

Fig. 1A DNA and Amino Acid Sequence of Variable Region of FR1-H7 Heavy Chain

Heavy chain variable region sequence (cDNA)

ATGGCCGAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGG
GCCTCAGTGAAGGTTTCCTGCAAGGTTTCTGGATACACCTTCACCGACTACTA
CATGCACTGGGTGCAACAGGCCCTGGAAAAGGGCTTGAGTGGATGGGACTT
GTTGATCCTGAAGATGGTGAAACAATCTACGCAGAGAAGTTCCAGGGCAGAG
TCACCATAACCGCGGACACGTCTACAGACACAGCCTACATGGAGCTGAGCAG
CCTGAGATCTGAGGACACGGCCGTGTATTACTGTGCGAGAGATGACTACATG
GACGTCTGGGGCAAAGGCACCCTGGTCACCGTCTCAAGCGCCTCCACCAAGG
GCCCA

Heavy chain variable region sequence (amino acid)

MAEVQLVQSGAEVKKPGASVKVSCKVSGYTFTDYYMHWVQQAPGKGLEWMG
LVDPEDGE TIYAEKFQGRVTITADTSTD TAYMELSSLRSED TAVYYCARD D YMD
VWGKGTL VTVSSASTKGP

Best Available Copy

Fig. 1B DNA and Amino Acid Sequence of Variable Region of FR1-H7 light Chain

Light chain variable region sequence (cDNA)

CTTGAAACGACACTCACGCAGTCTCCAGACACCCTGTCTTTGTCTCCAGGAGA
AGGAGCCACCCTCTCCTGTAGGGGCCAGTCAGAGTGTTAGCGGCAGTGCGTTG
GCCTGGTACCAGCAGAAACCTGGCCAGGCTCCCAGACTCCTCATCTATGATG
CATCCAGTAGGGCCACTGGCGTCCCAGACAGGTTTCAGTGGCAGTGGGTCTGG
GGCAGACTTCAGTCTCACCATCAGCAGACTGGAGCCTGAAGATTTTGCAGTG
TATTCCTGTCAGCAATATGGTAGCTCACCTCTCACTTTCGGCCCTGGGACCAA
AGTGGATGTCAAACGAACTGTGGCTGCACCATCTGTCTTCATCTTCCCGCCAT
CTGATGAGCAGTTGAAATCTGGAACTGCCTCTGTTGTGTGCCTGCTGAATAAC
TTCTATCCCAGAGAGGCCCAAAGTACAGTGGAAGGTGGATT

Light chain variable region sequence (amino acid)

LETTLTQSPDTLSLSPGEGATLSCRASQSVSGSALAWYQQKPGQAPRLLIYDASS
RATGVPDRFSGSGSGADFSLTISRLEPEDFAVYSCQQYGSSPLTFGPGTKVDVKR
TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVD

Fig. 1C CDRs For FR1-H7 Nucleic Acid Sequences

VH (human heavy chain subclass I)

CDR1 GACTACTACATGCAC

CDR2 CTTGTTGATCCTGAAGATGGTGAAACAATCTACGCAGAGAAGTTCCAGGGC

CDR3 GATGACTACATGGACGTC

VL (human kappa light chain subgroup III)

CDR1 AGGGCCAGTCAGAGTGTTAGCGGCAGTGC GTTGGCC

CDR2 GATGCATCCAGTAGGGCCACT

CDR3 CAGCAATATGGTAGCTCACCTCTCACT

Fig. 1D CDRs For FR1-H7 Amino Acid Sequences

VH (human heavy chain subclass I)

CDR1	DYYMH
CDR2	LVDPEDGETIYAEKFQG
CDR3	DDYMDV

VL (human kappa light chain subgroup III)

CDR1	RASQSVSGSALA		
CDR2	DASSRAT		
		CDR3	QQYGSSPLT

Fig. 2A DNA and Amino Acid Sequence of Variable Region of FR1-A1 Heavy Chain

Heavy chain variable region sequence (cDNA)

ATGGCCCAGGTCCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGT
CCTCGGTGAAGGTCTCCTGCAAGGCTTCTGGATCGACCTTCACCGGCTACTAT
ATGCACTGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTGGATGGGAAGG
ATCATCCCTATCCTTGGTATAGCAAACCTACGCACAGAAGTTCCAGGGCAGAG
TCACGATTACCGCGGACAAATCCACGAGCACAGCCTACATGGAGCTGAGCAG
CCTGAGATCTGAGGACACGGCCGTGTACTACTGTGCGAGAGGAGGAGATCTG
GGCGGTATGGACGTCTGGGGCCAAGGGA

Heavy chain variable region sequence (amino acid)

MAQVQLVQSGAEVKKPGSSVKVSC¹KASGQTFTGY²YMH³WVRQAPGQGLEWMG
RIIPILGIAN⁴YAQKFQGRVTITADKSTSTAYMELSSLRSED⁵TA⁶VYYCARGGDLGG
MDVWGQG

Fig. 2B DNA and Amino Acid Sequence of Variable Region of FR1-A light Chain

Light chain variable region sequence (cDNA)

CTTGAAATTGTGCTGACTCAGTCTCCACTCTCCCTGCCCCGTCACCCCTGGAGA
GCCGGCCTCCATCTCCTGCAGGTCTAGTCAGAGCCTCCGGCATAGTAATGGA
TACAACTATTTGGATTGGTACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCT
GATCTATTTGGCTTCTAATCGGGCCTCCGGGGTCCCTGACAGGTTCAGTGGCA
GTGGATCAGGCACAGATTTTACACTGAAAATCAGCAGAGTGGAGGCTGAGGA
TGTTGGGGTTTATTACTGCATGCAAGCTCTACAAATTCCTCCGACTTTCGGCC
CTGGGACCAAAGTGGATATCAAACGAACTGTGGCTGCA

Light chain variable region sequence (amino acid)

LEIVLTQSPLSLPVTGPGEPAISCRSSQSLRHSNGYNYLDWYLQKPGQSPQLLIYL
ASNRASGVDPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQIPPTFGPGTKVD
IKRTVAA

Fig. 2C CDRs For FR1-A1 Nucleic Acid Sequences

VH (human heavy chain subclass I)

CDR1 GGCTACTATATGCAC

CDR2 AGGATCATCCCTATCCTTGGTATAGCAAACCTACGCACAGAAGTTCCAGGGC

CDR3 GGAGGAGATCTGGGCGGTATGGACGTC

VL (human kappa light chain subgroup II)

CDR1 AGGTCTAGTCAGAGCCTCCGGCATAGTAATGGATACAACTATTTGGAT

CDR2 TTGGCTTCTAATCGGGCCTCC

CDR3 ATGCAAGCTCTACAAATTCCTCCGACT

Fig. 2D CDRs For FR1-A1 Amino Acid Sequences

VH (human heavy chain subclass I)

CDR1	GYMH
CDR2	RIIPILGIANYAQKFQG
CDR3	GGDLGGMDV

VL (human kappa light chain subgroup II)

CDR1	RSSQSLRHSNGYNYLD
CDR2	LASNRAS
CDR3	MQALQIPPT

Fig. 3

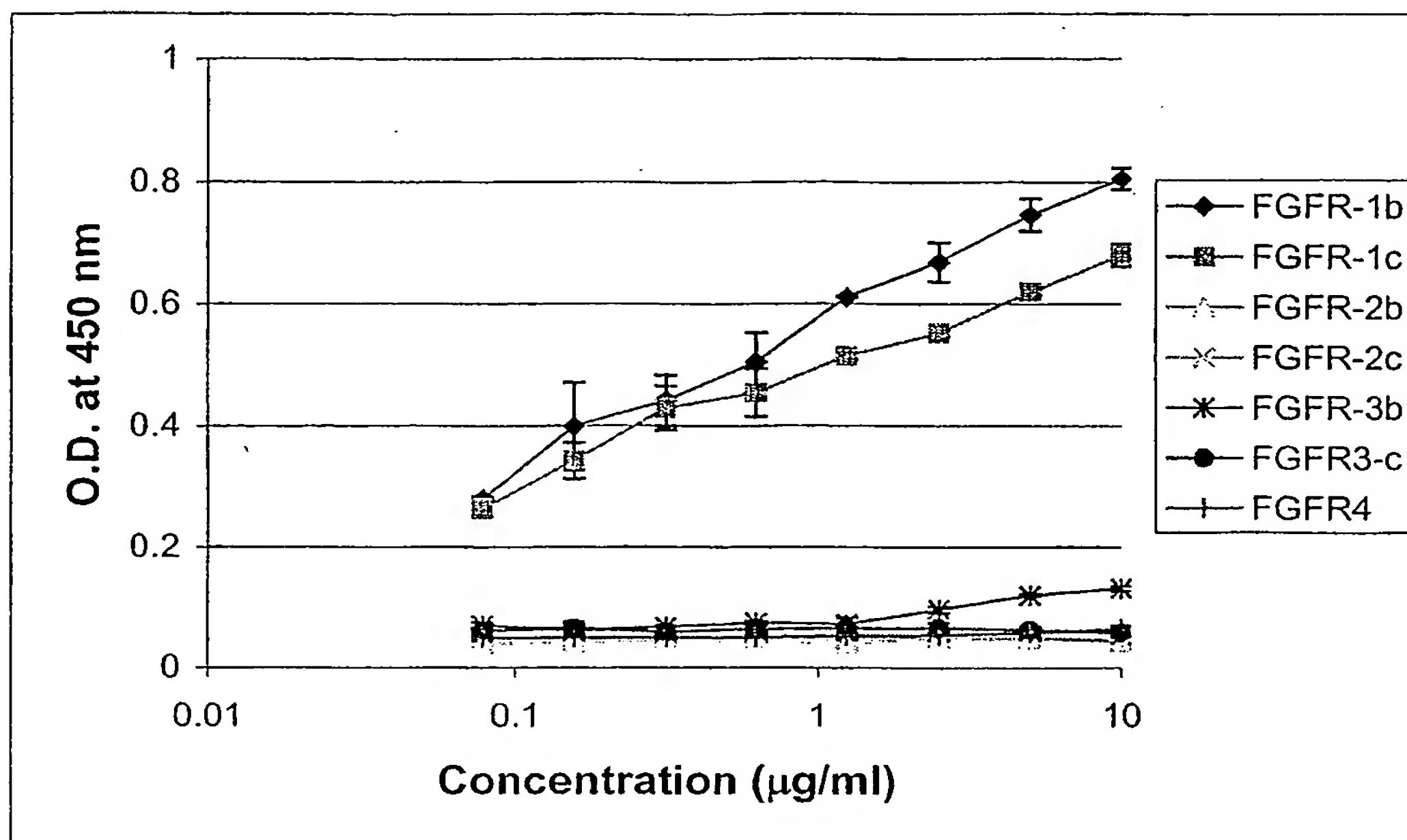


Fig. 4A

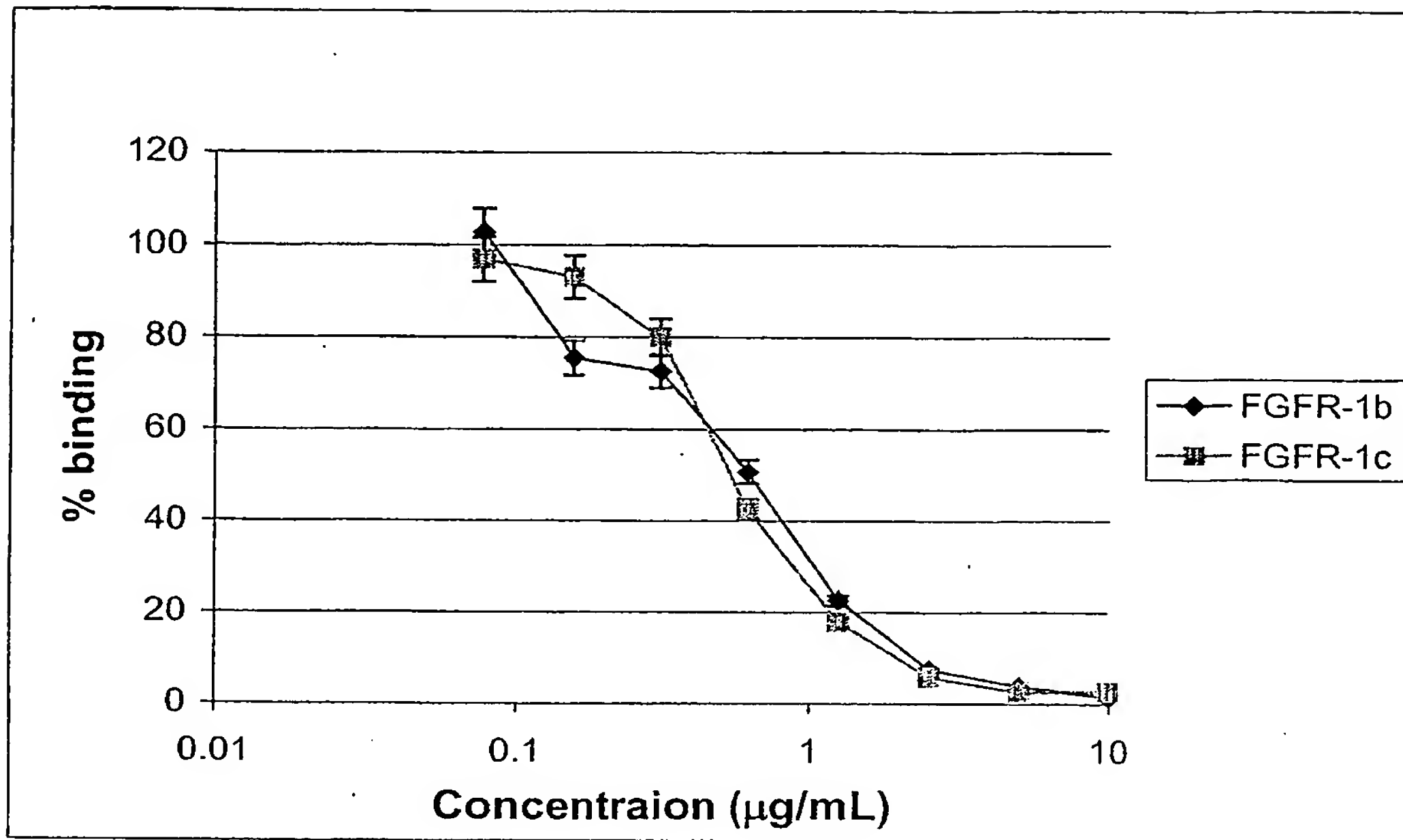


Fig. 4B

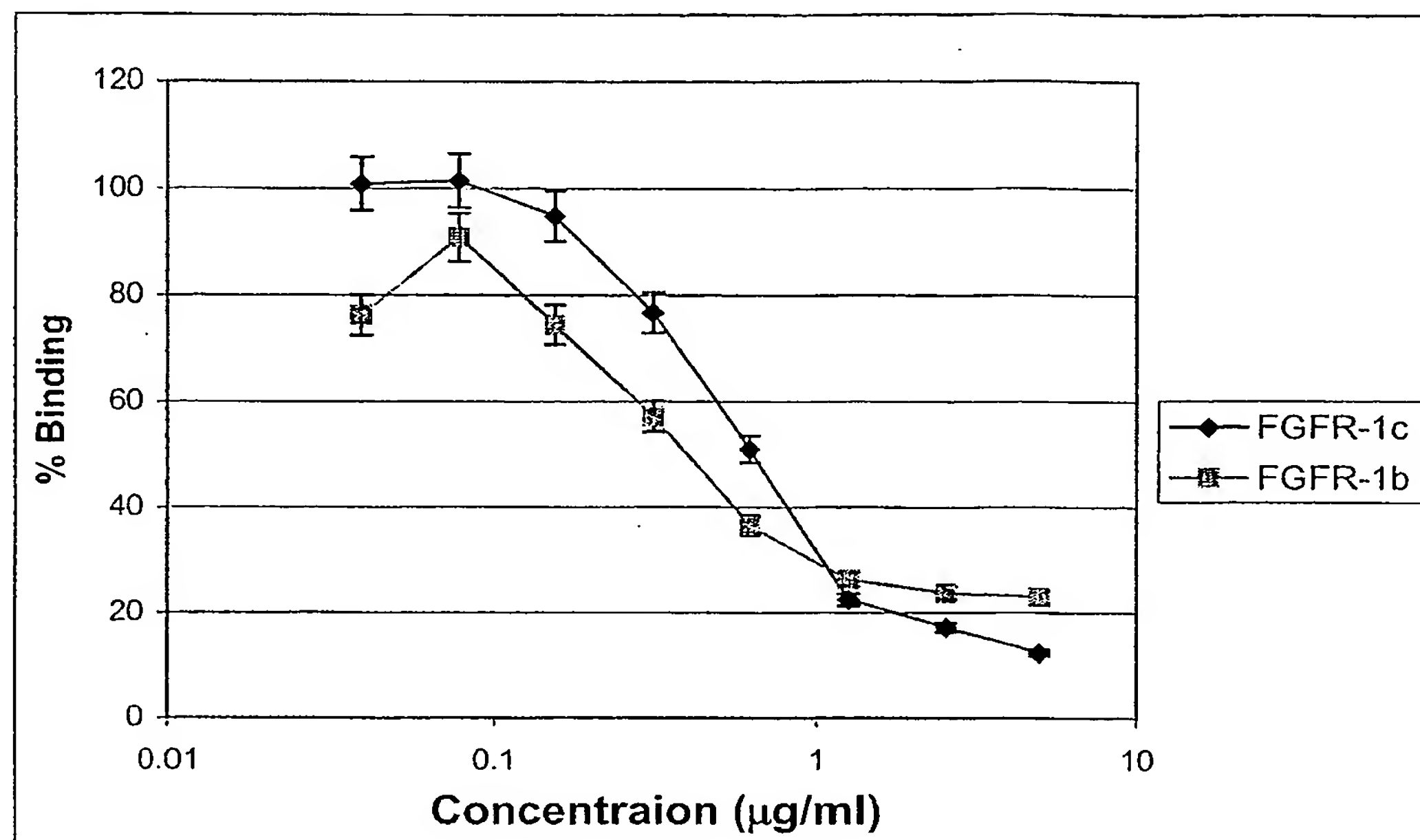


Fig. 5A

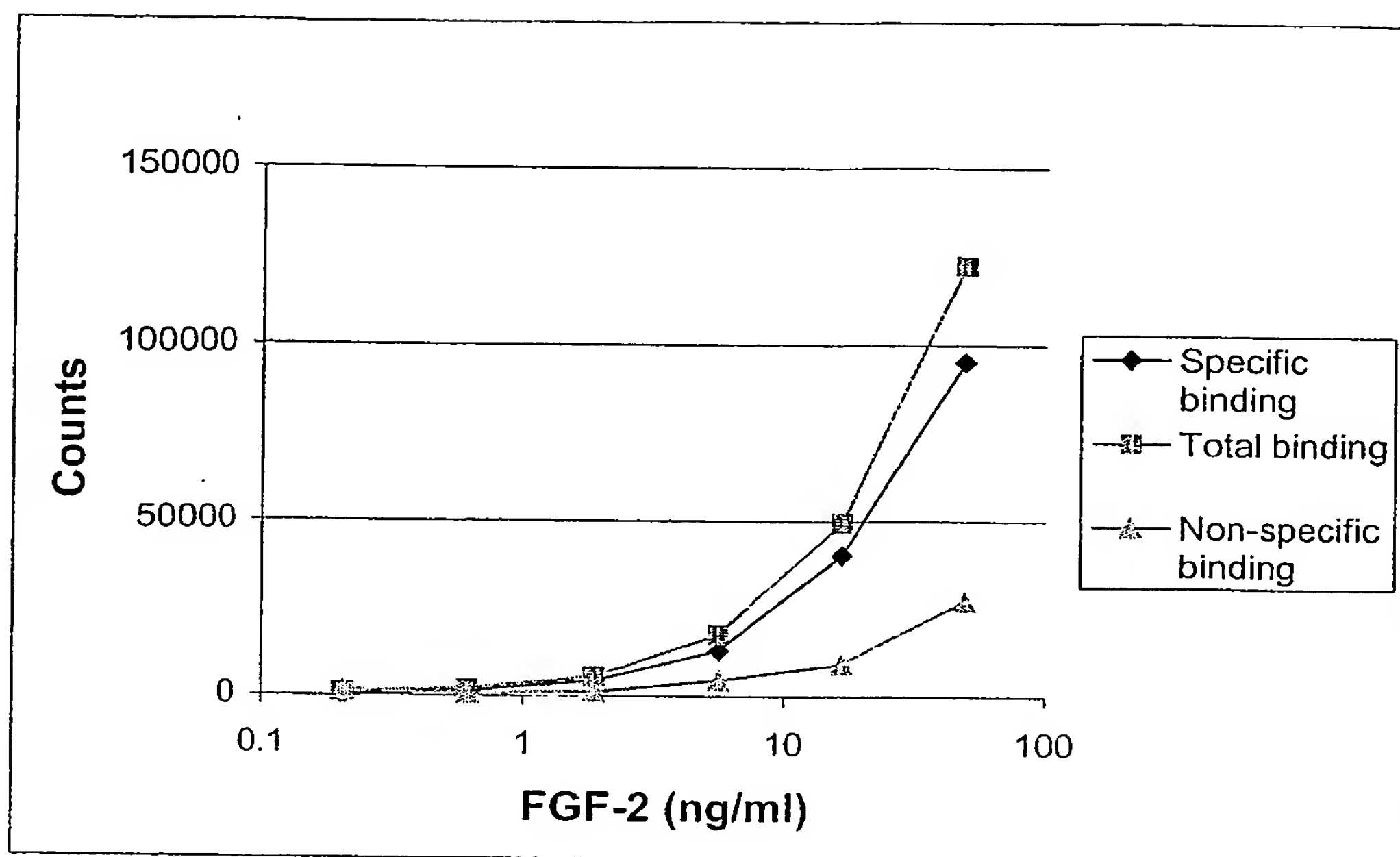


Fig. 5B

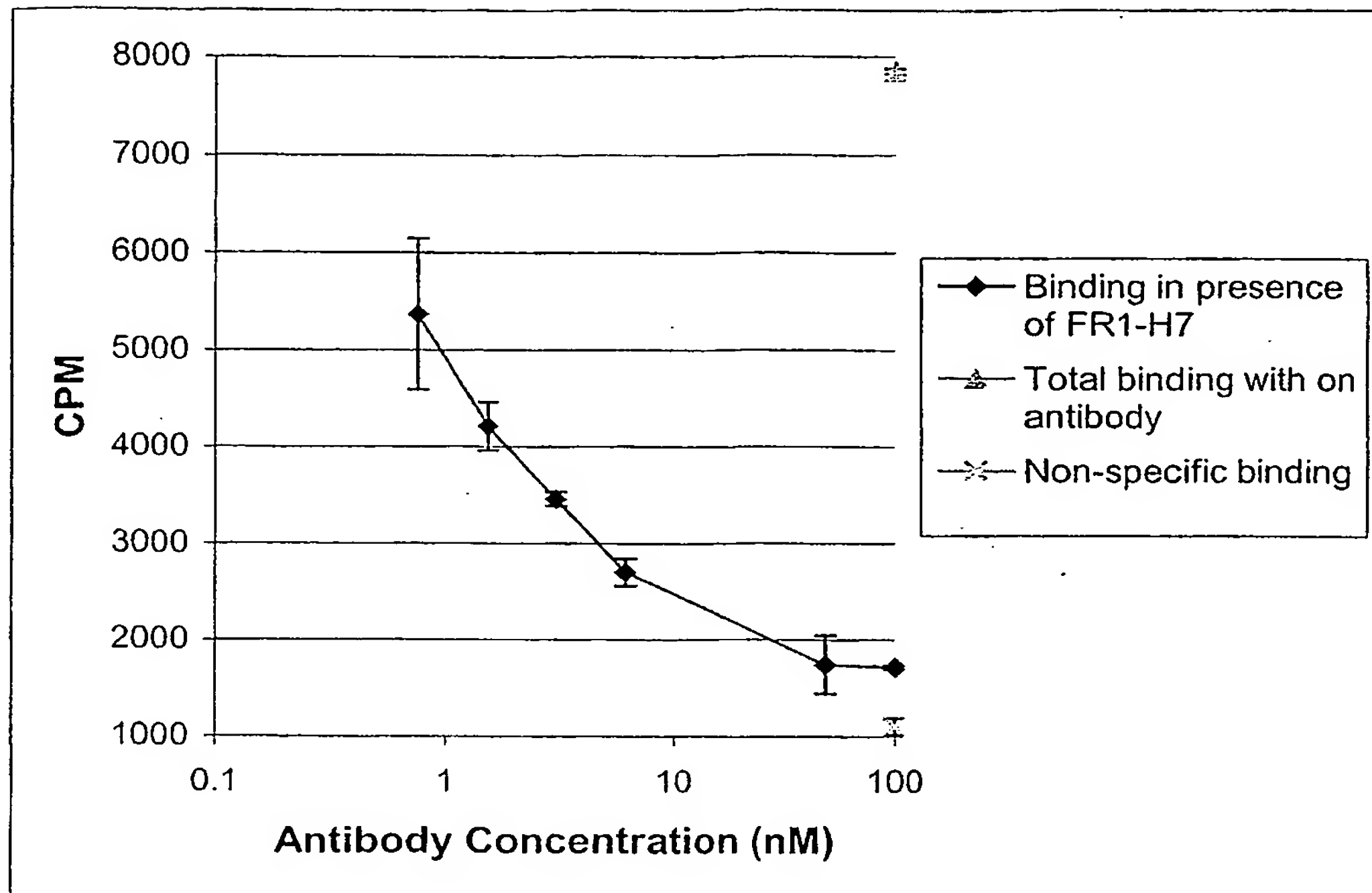


Fig. 6

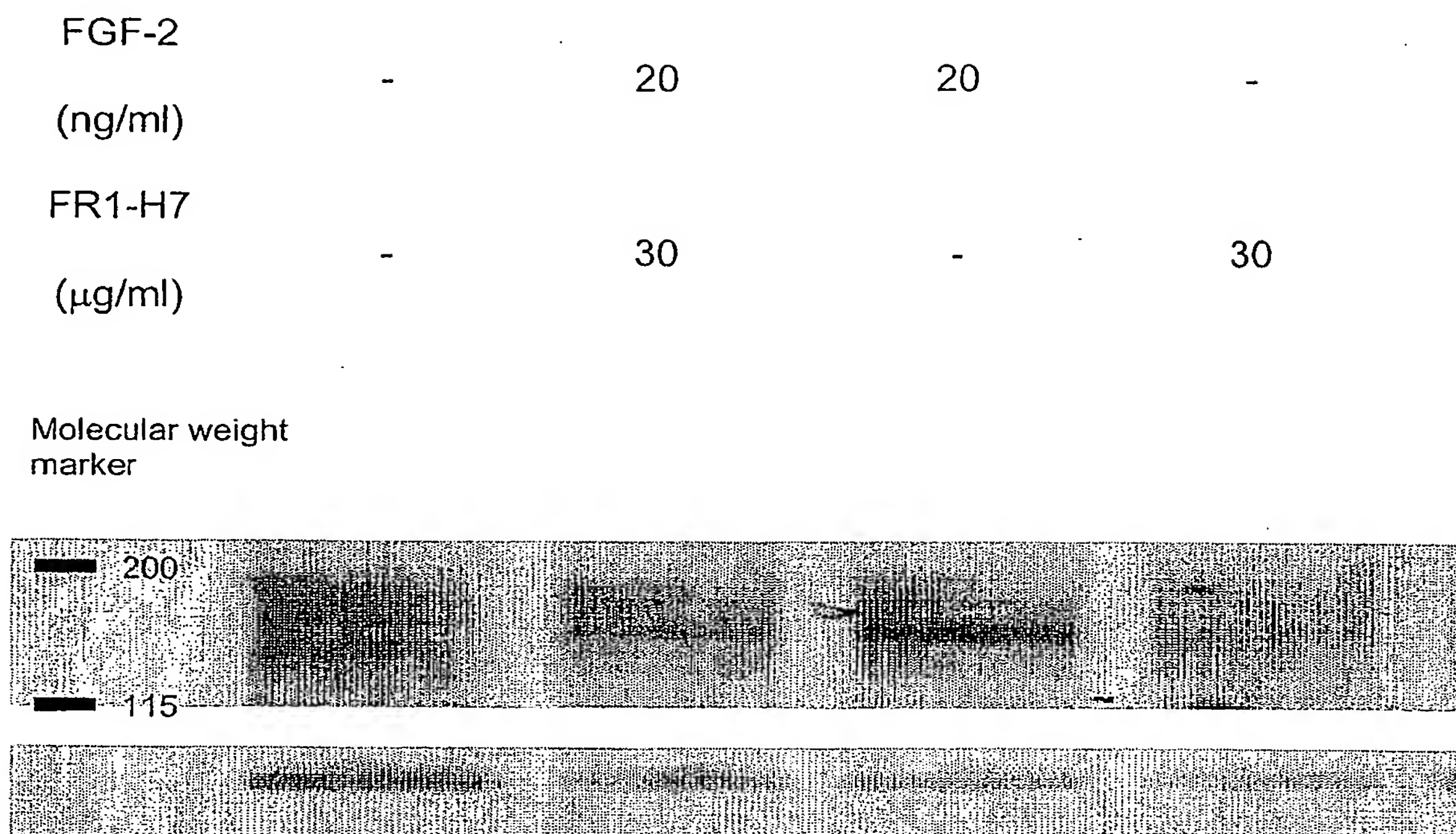


Fig. 7

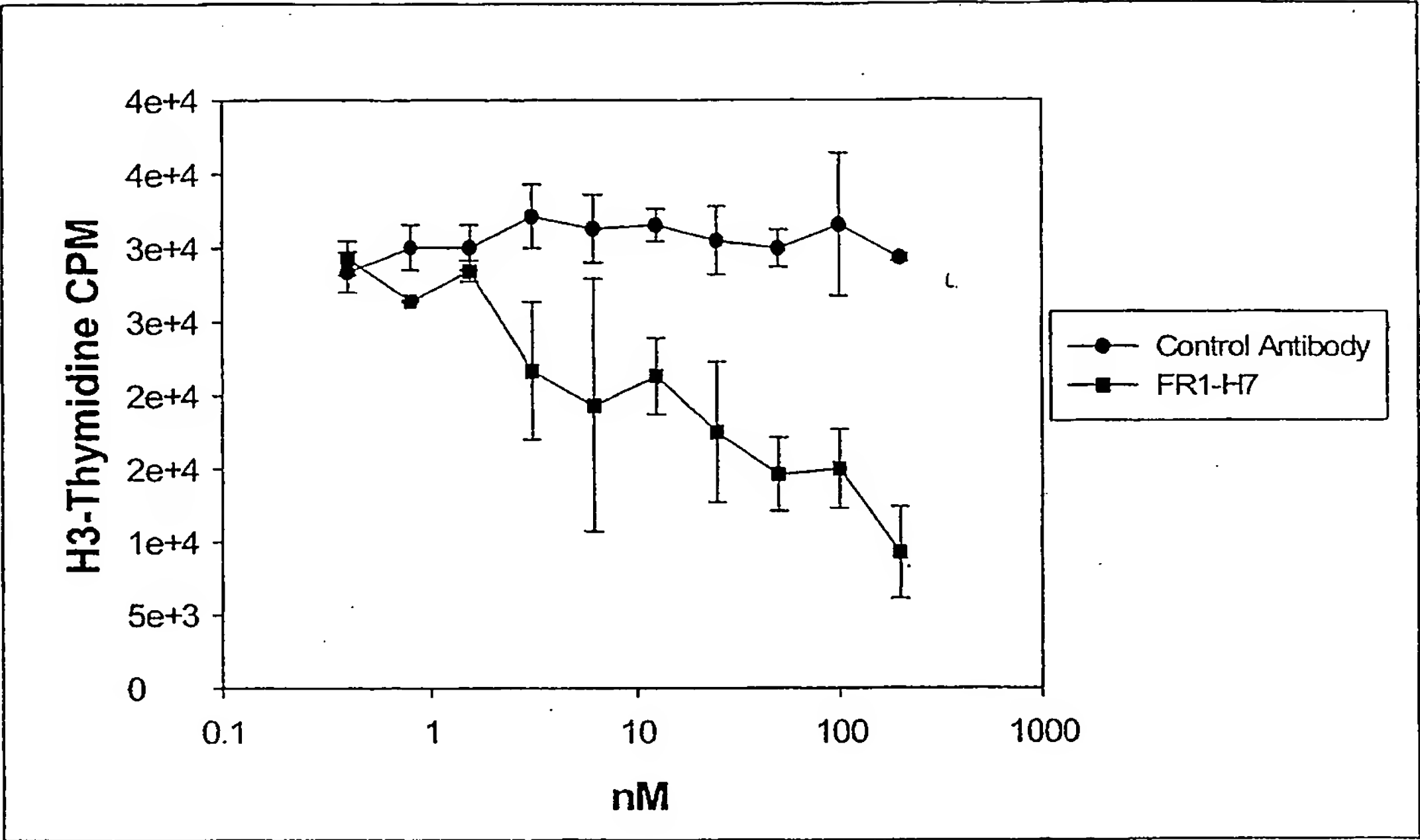


Fig. 8A

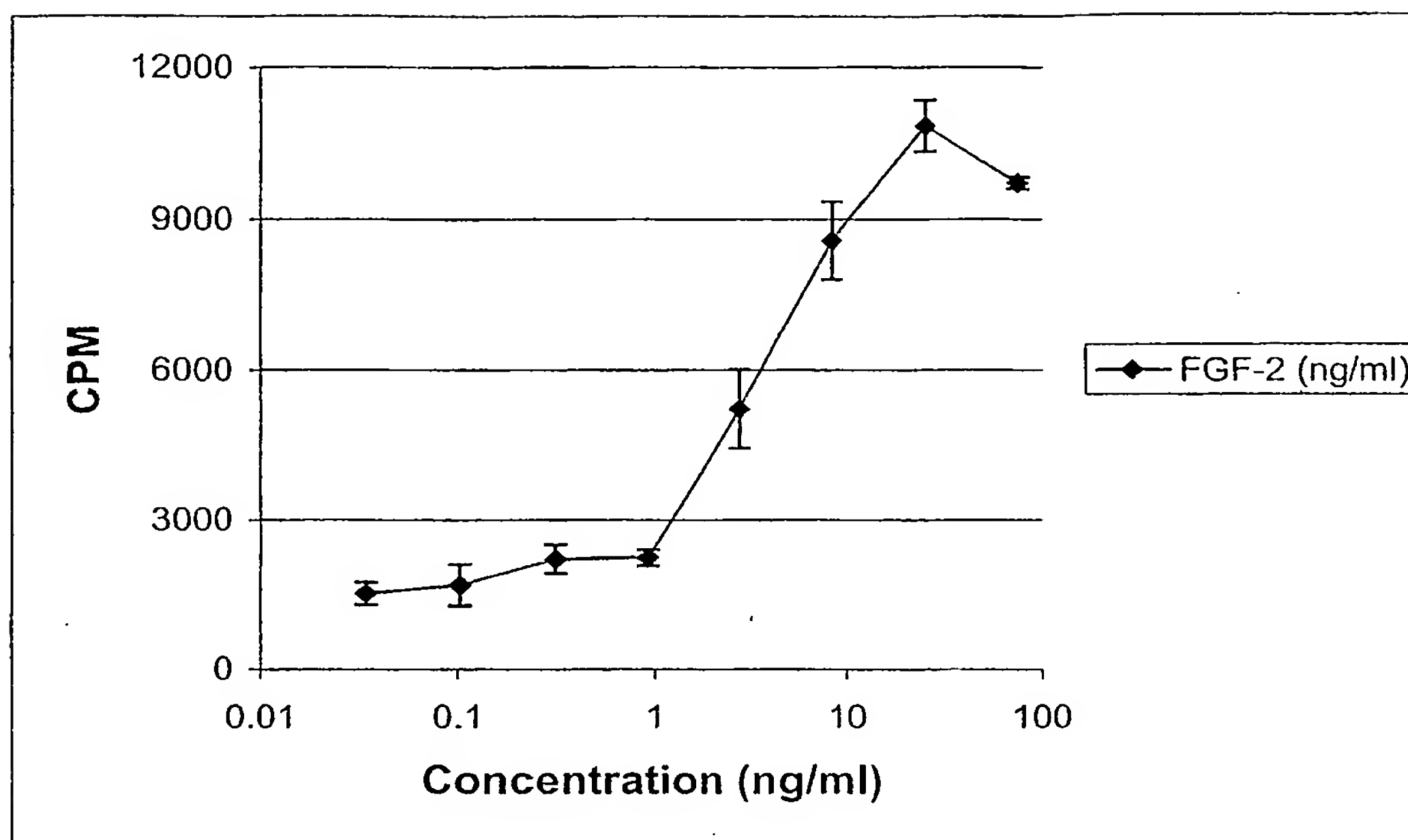


Fig. 8B

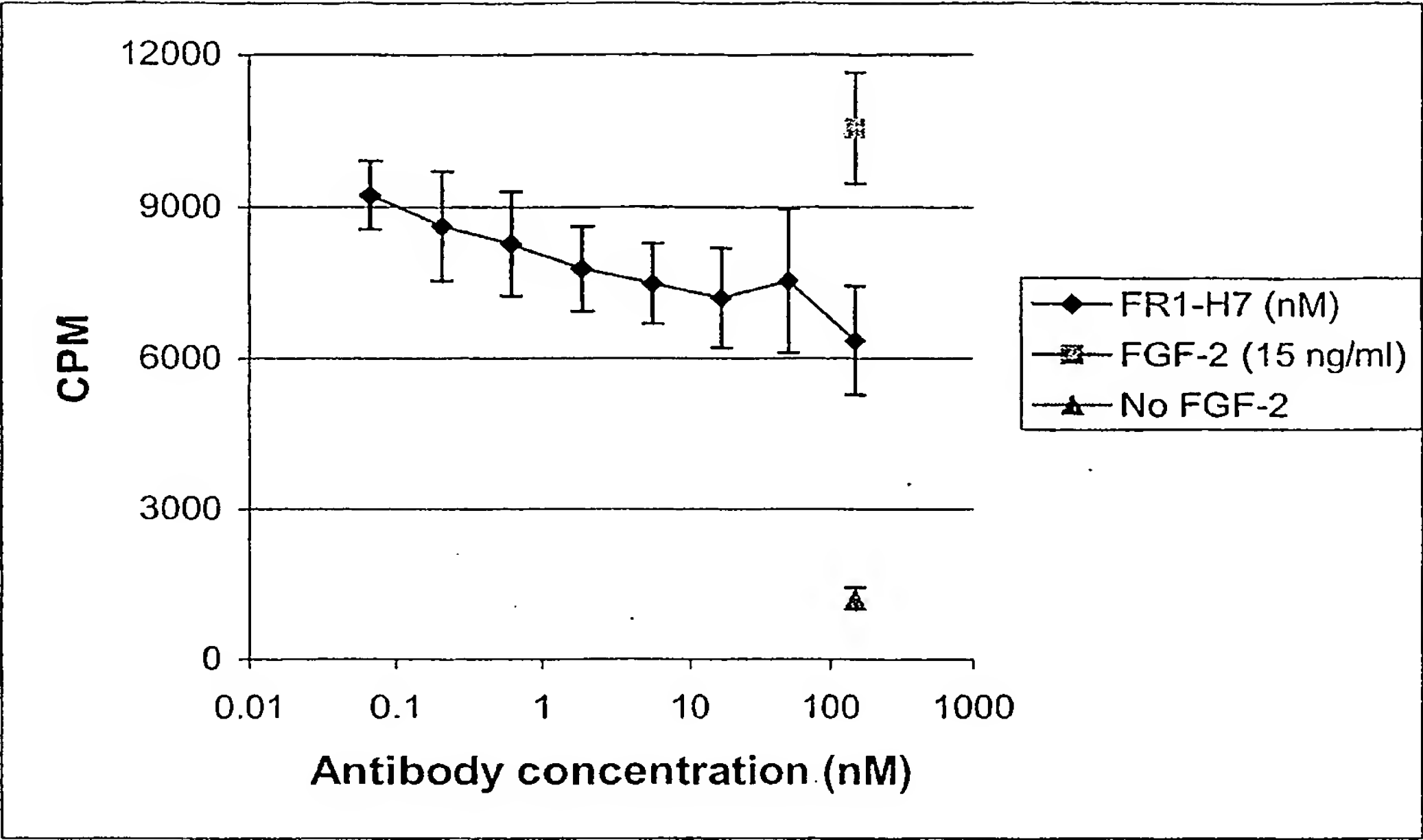
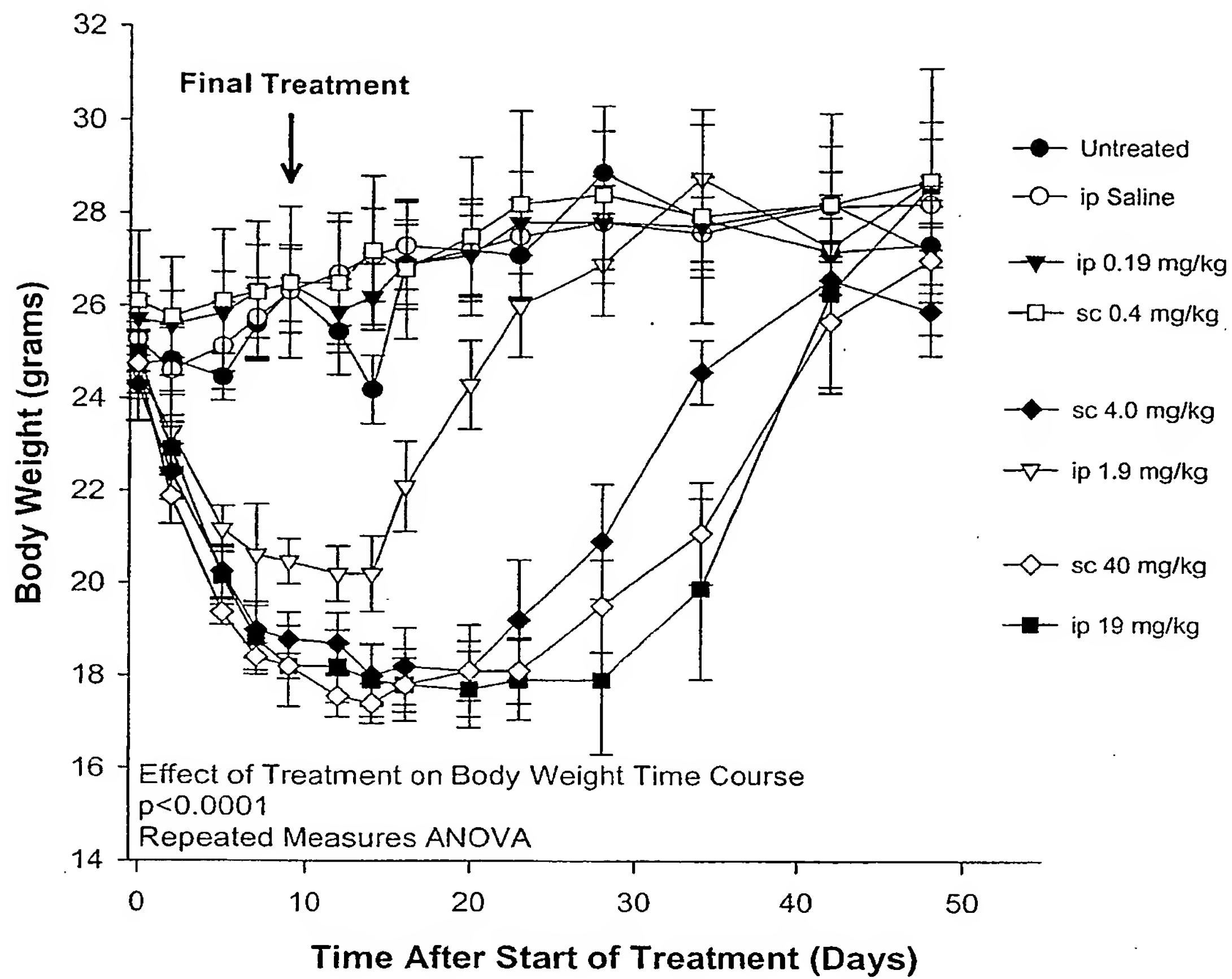


Fig. 9



*13 gram mouse euthanized

Fig. 10

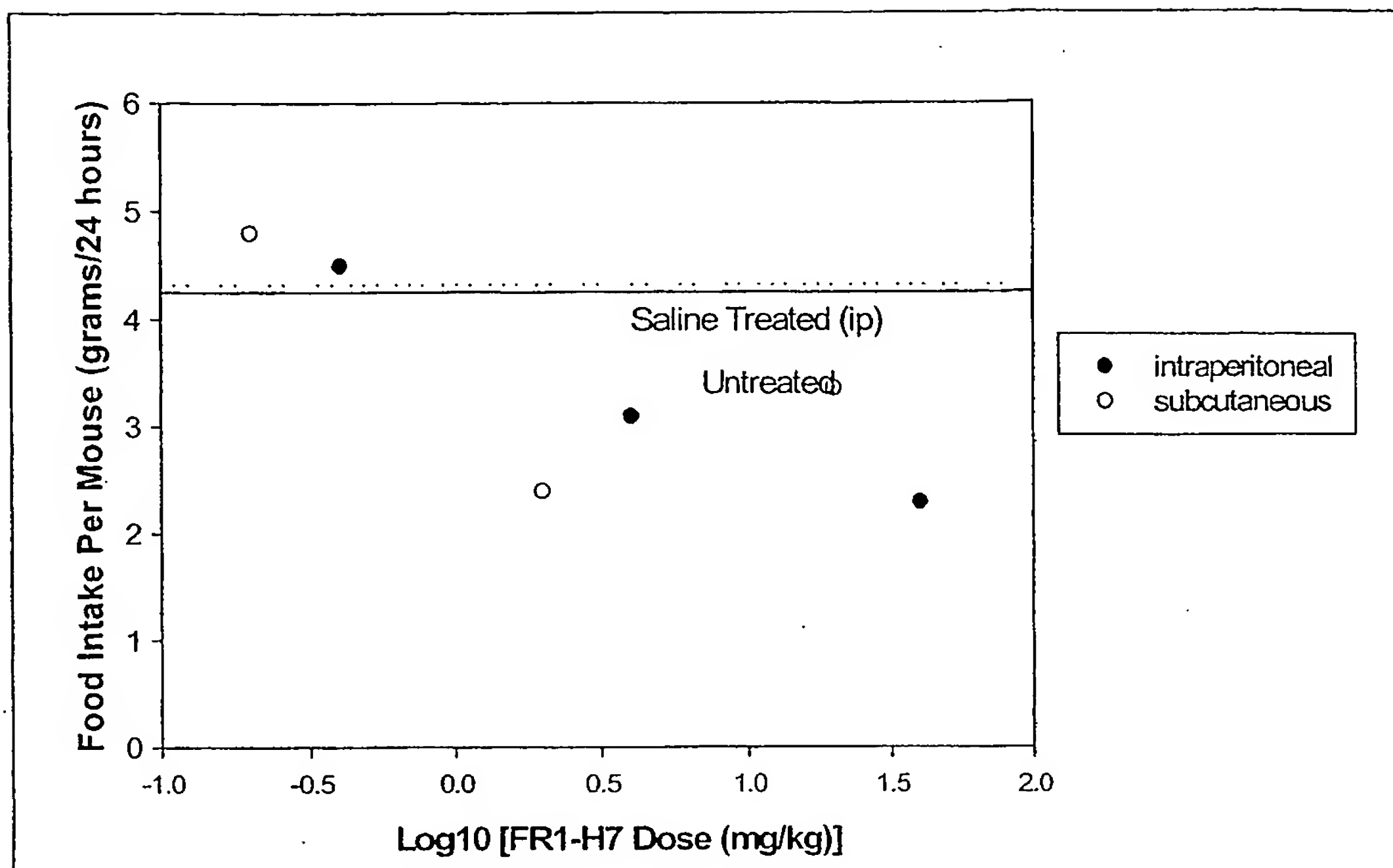


Fig. 11

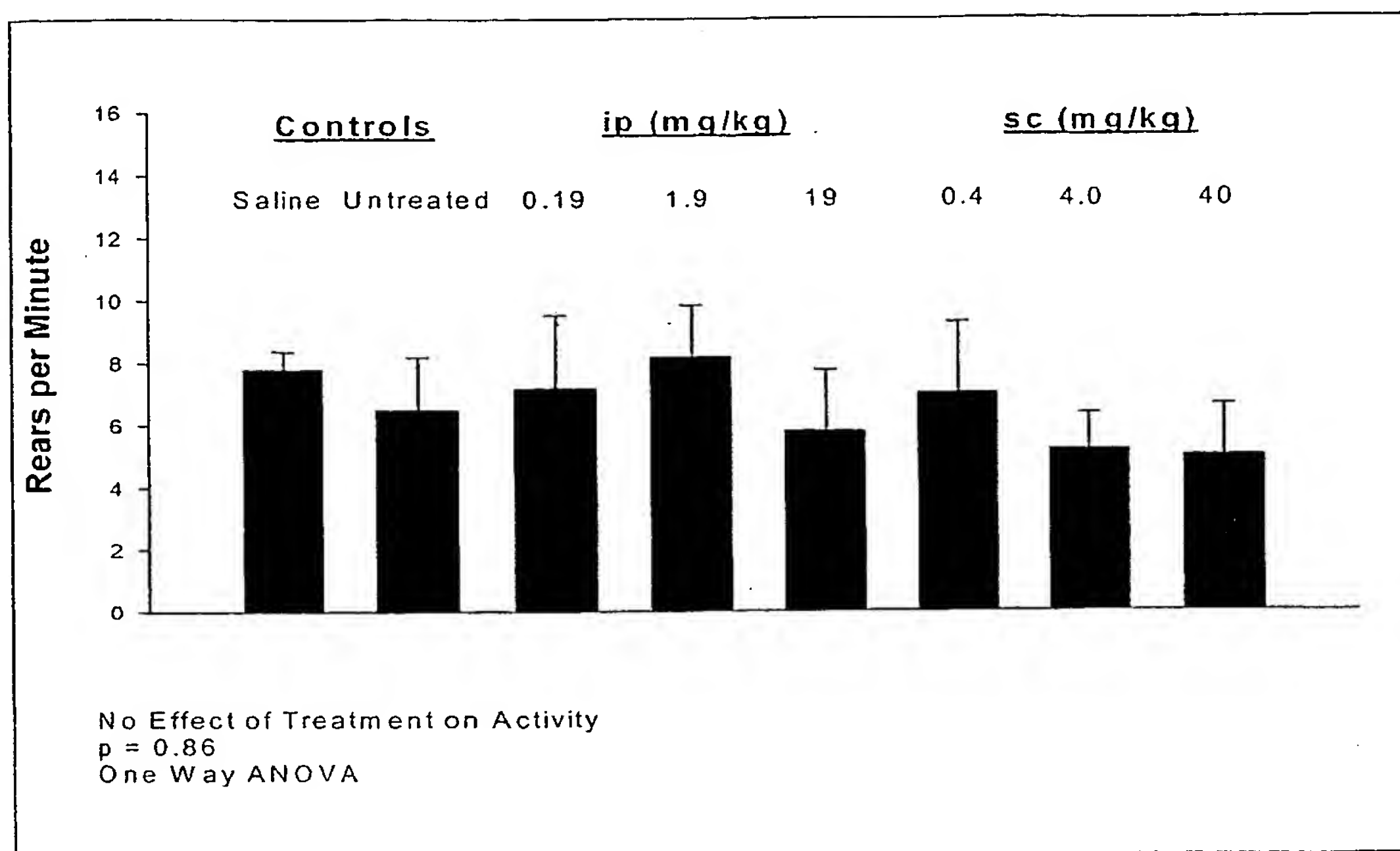


Fig. 12A

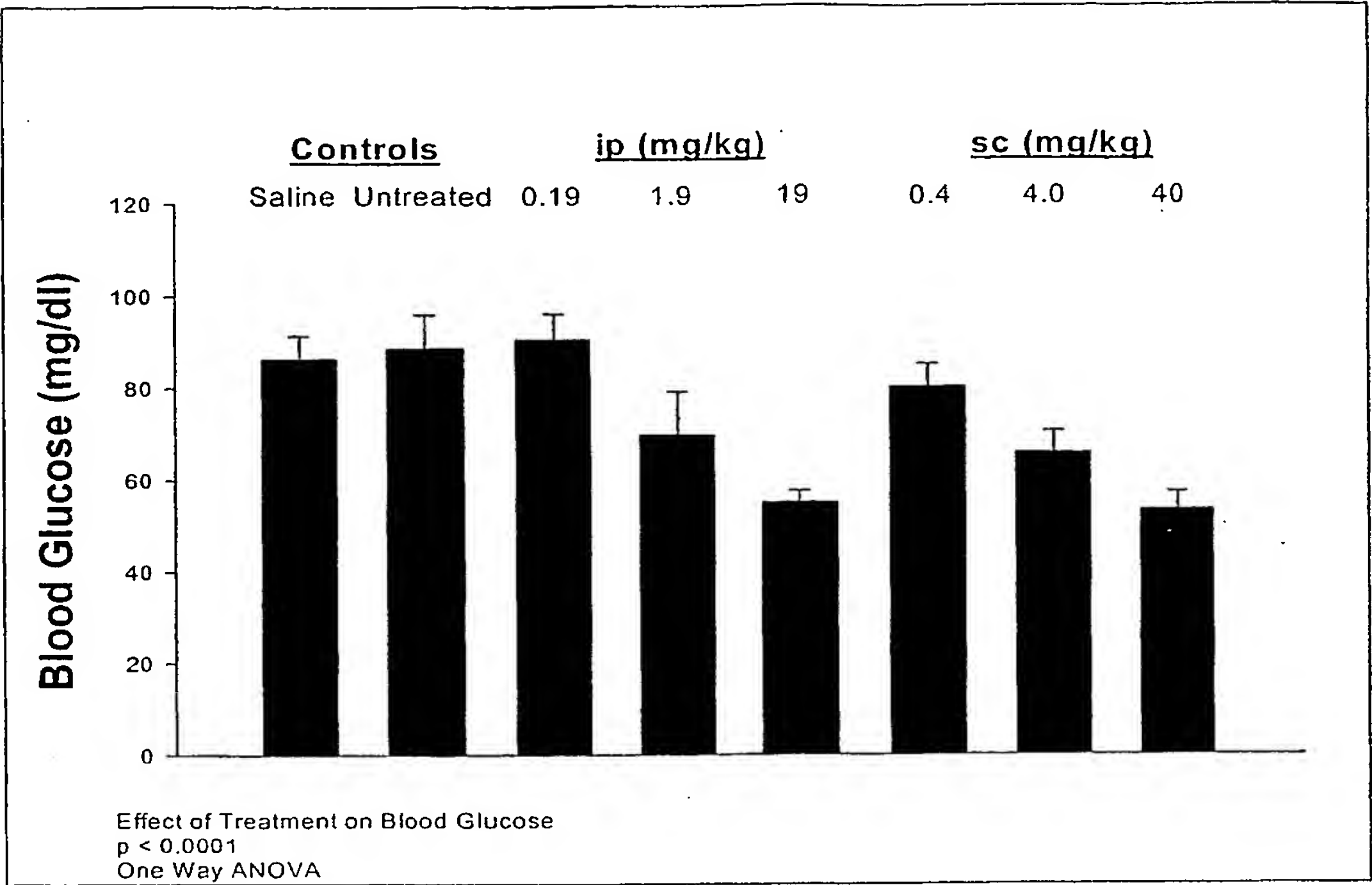


Fig. 12B

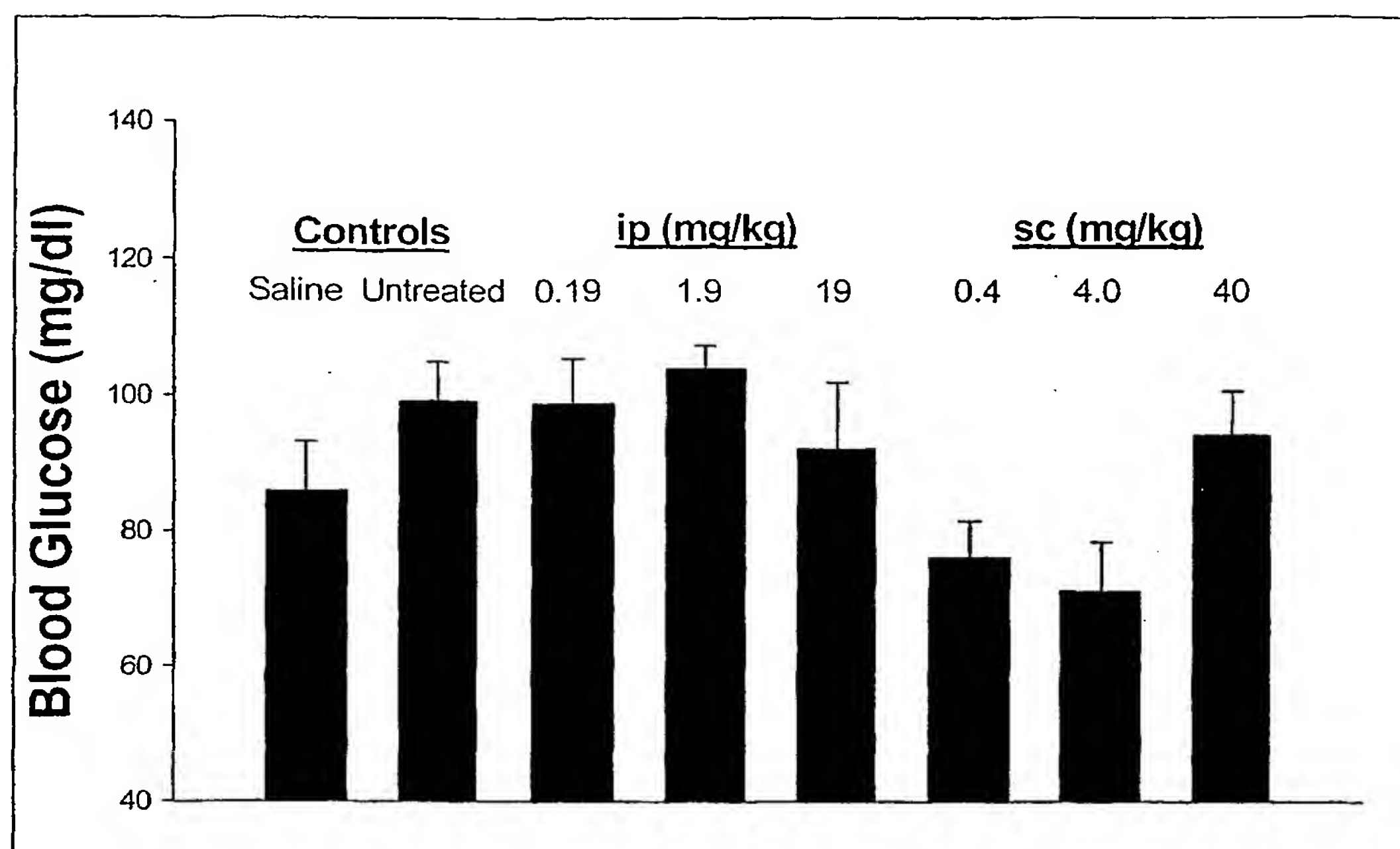


Fig. 13

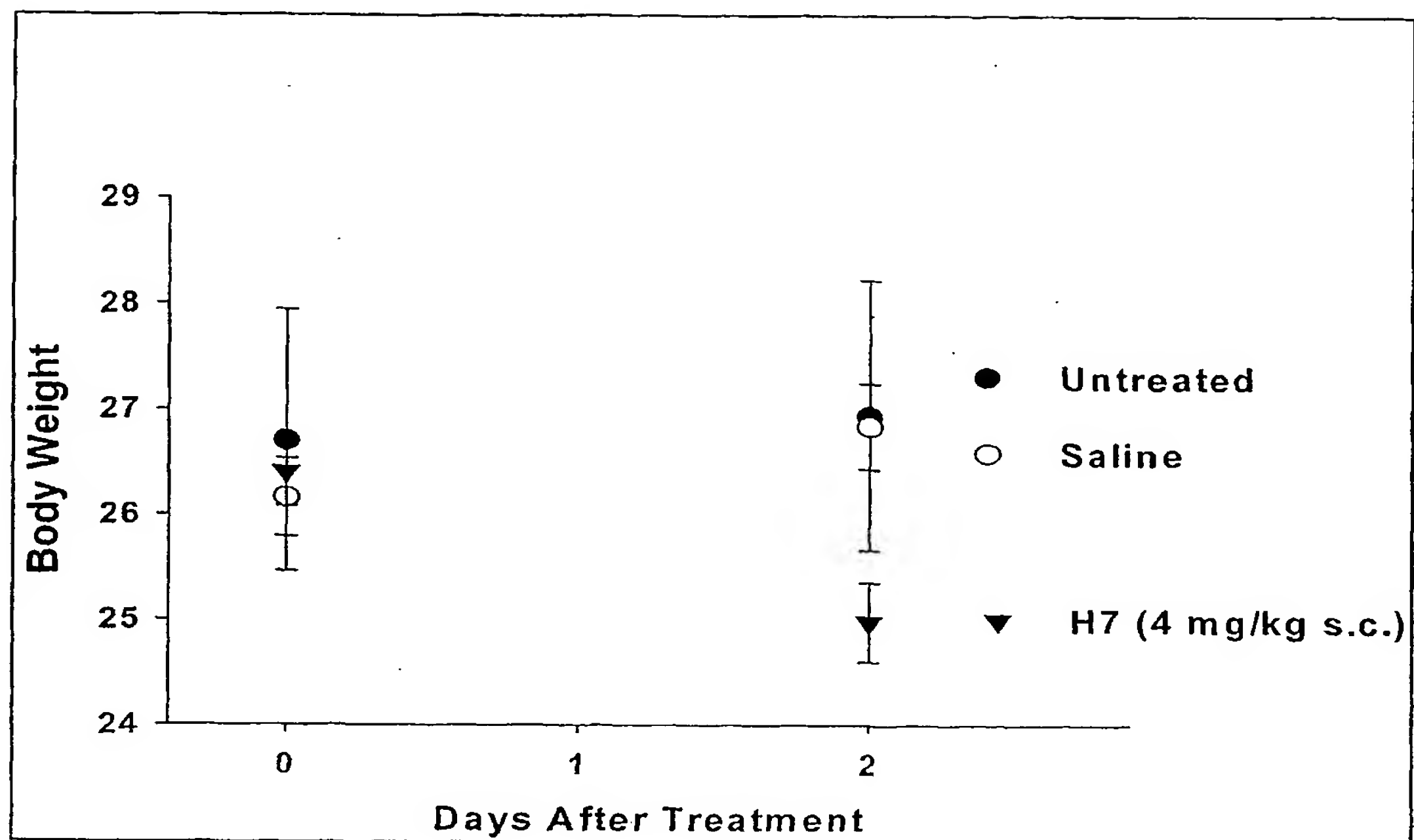


Fig. 14

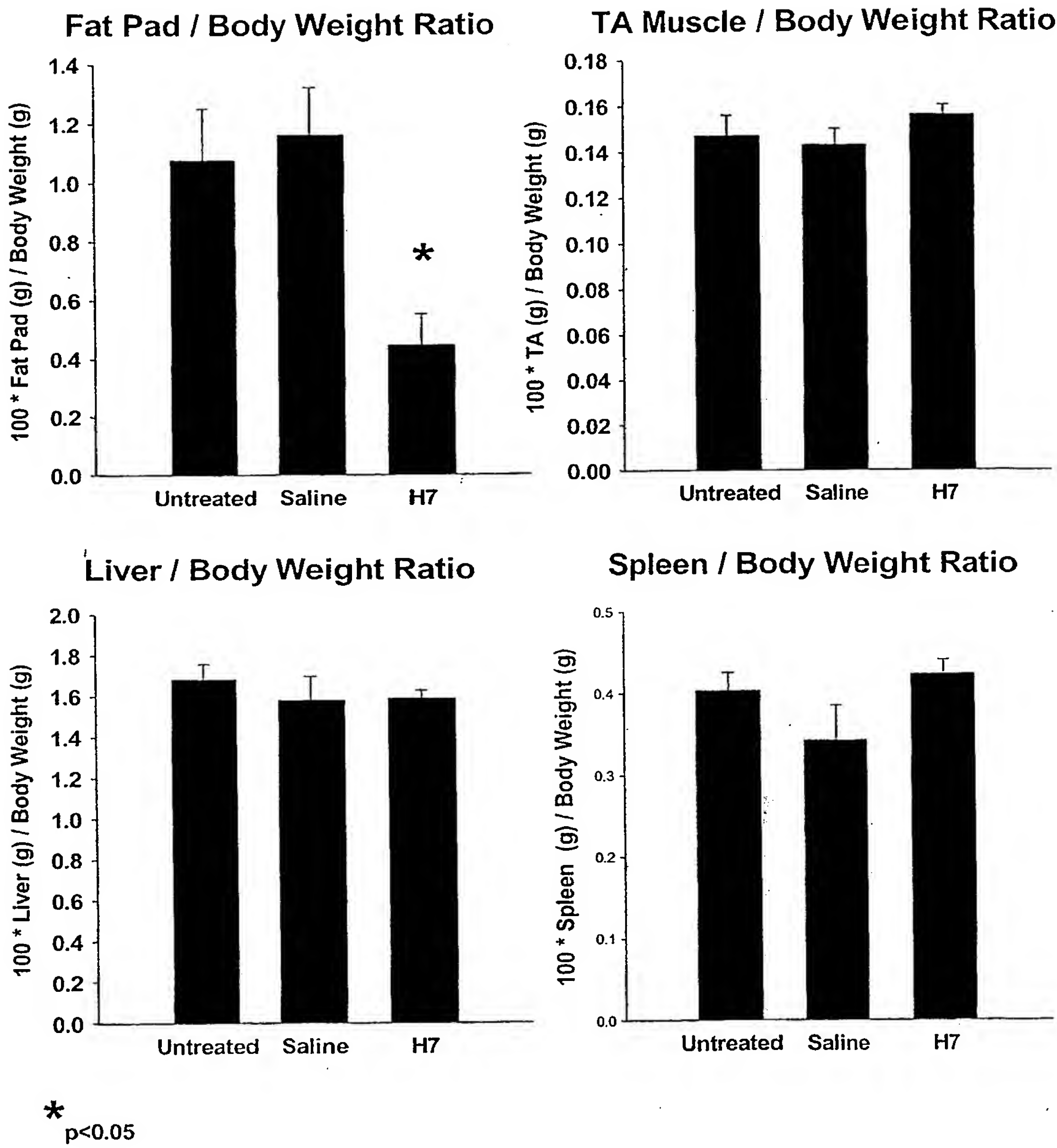


Fig. 15A

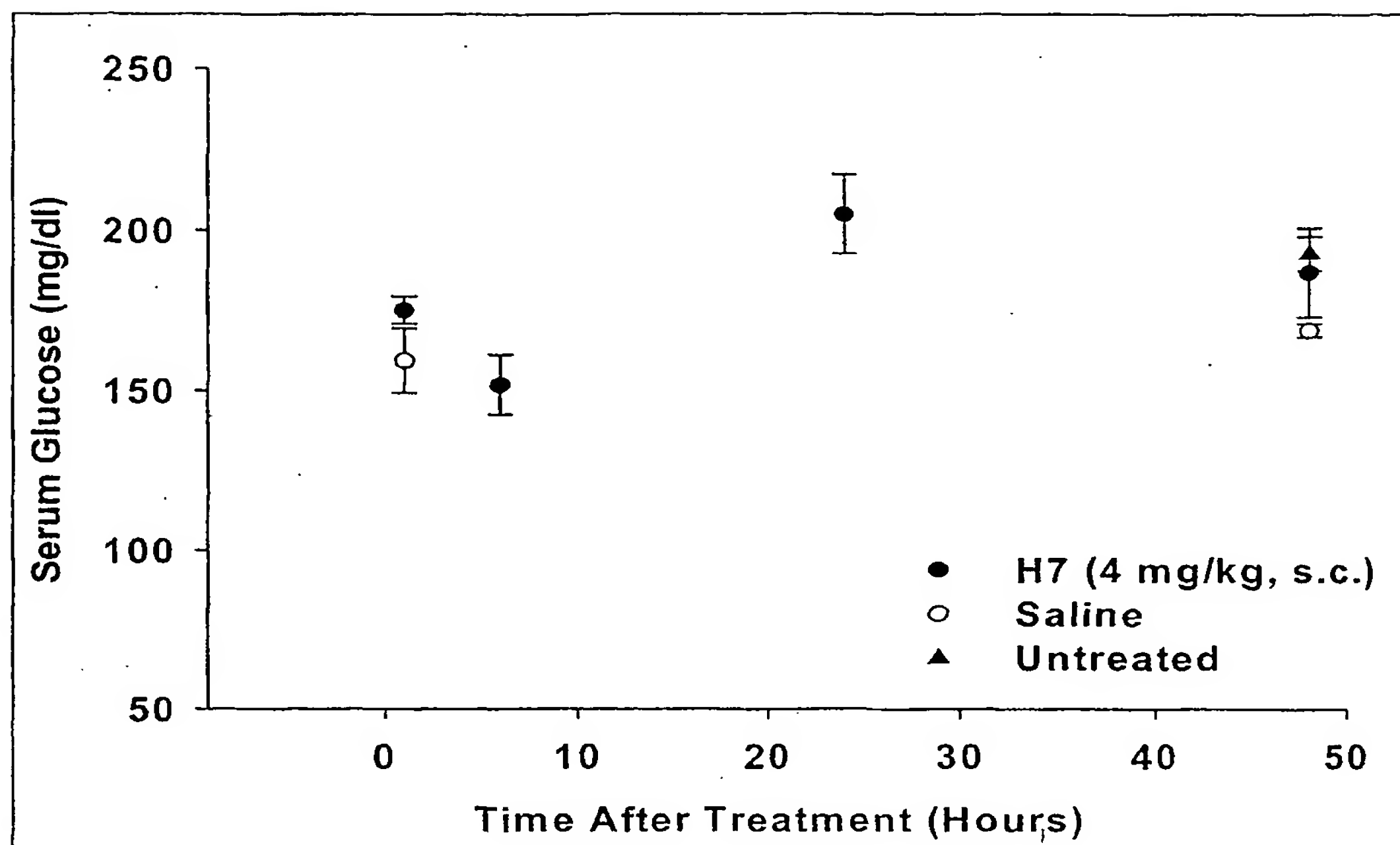


Fig. 15B

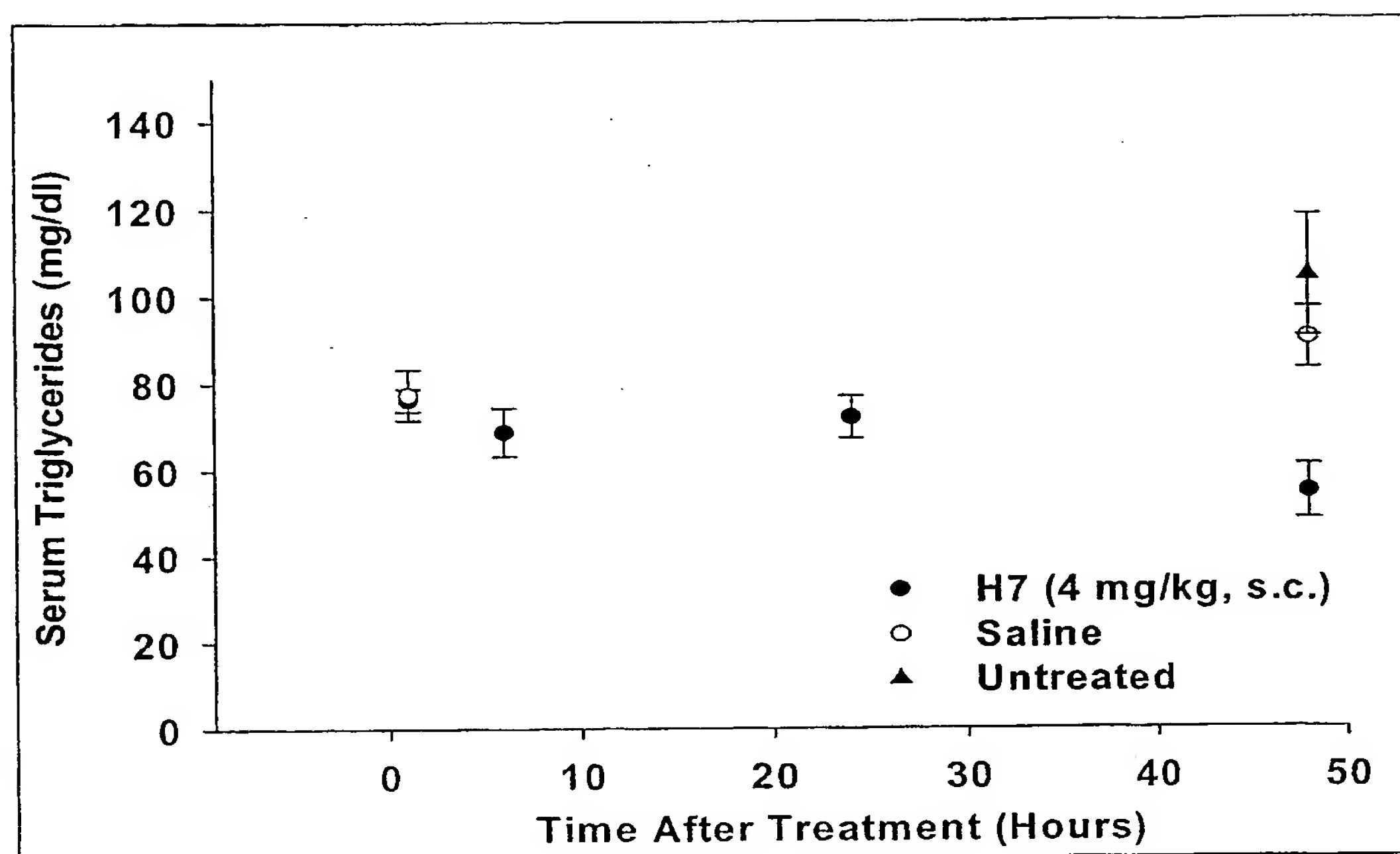


Fig. 15C

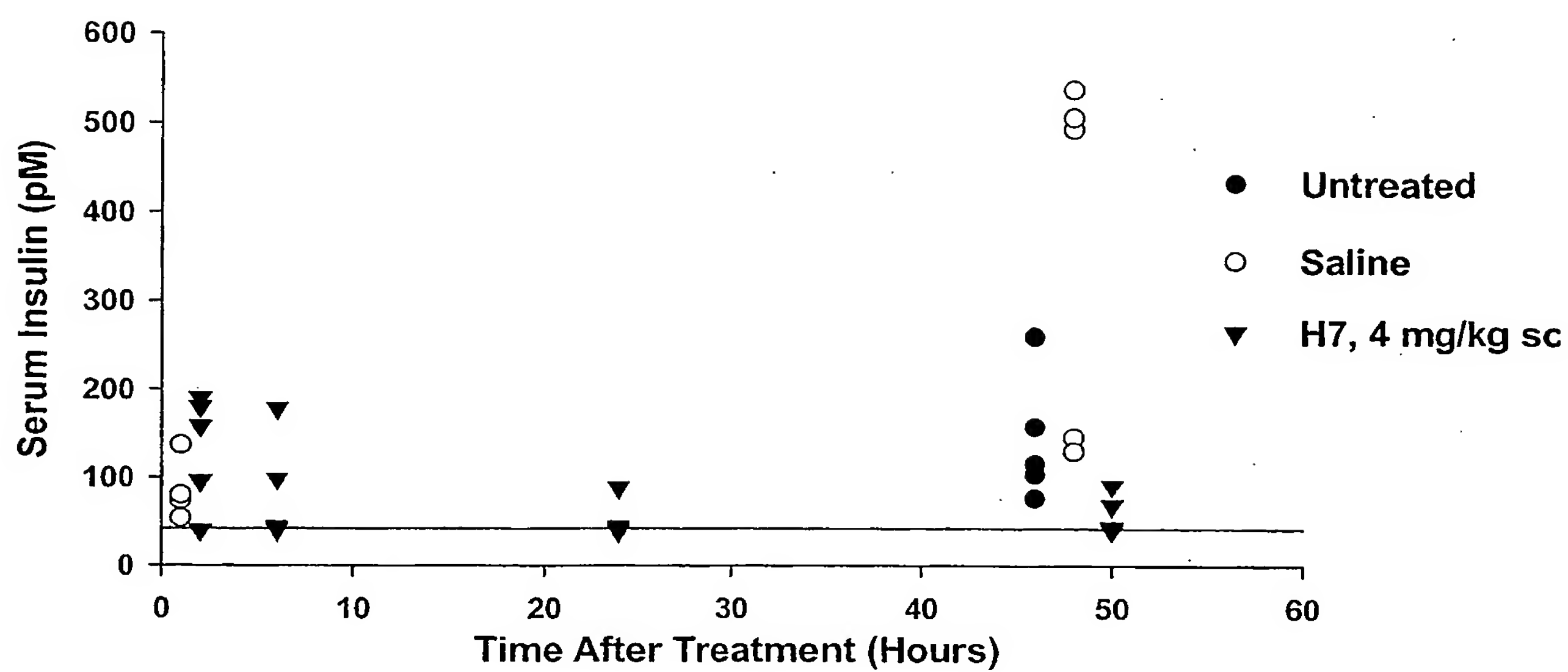


Fig. 15D

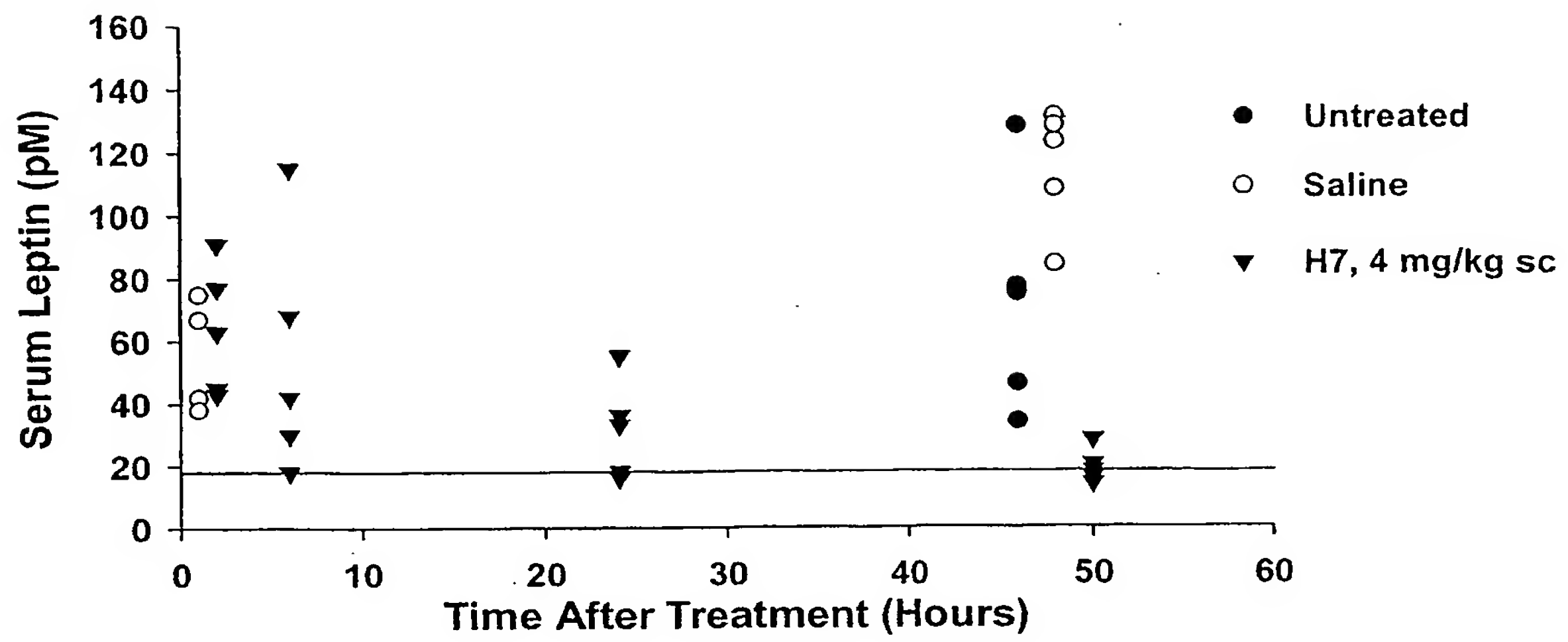


Fig. 16

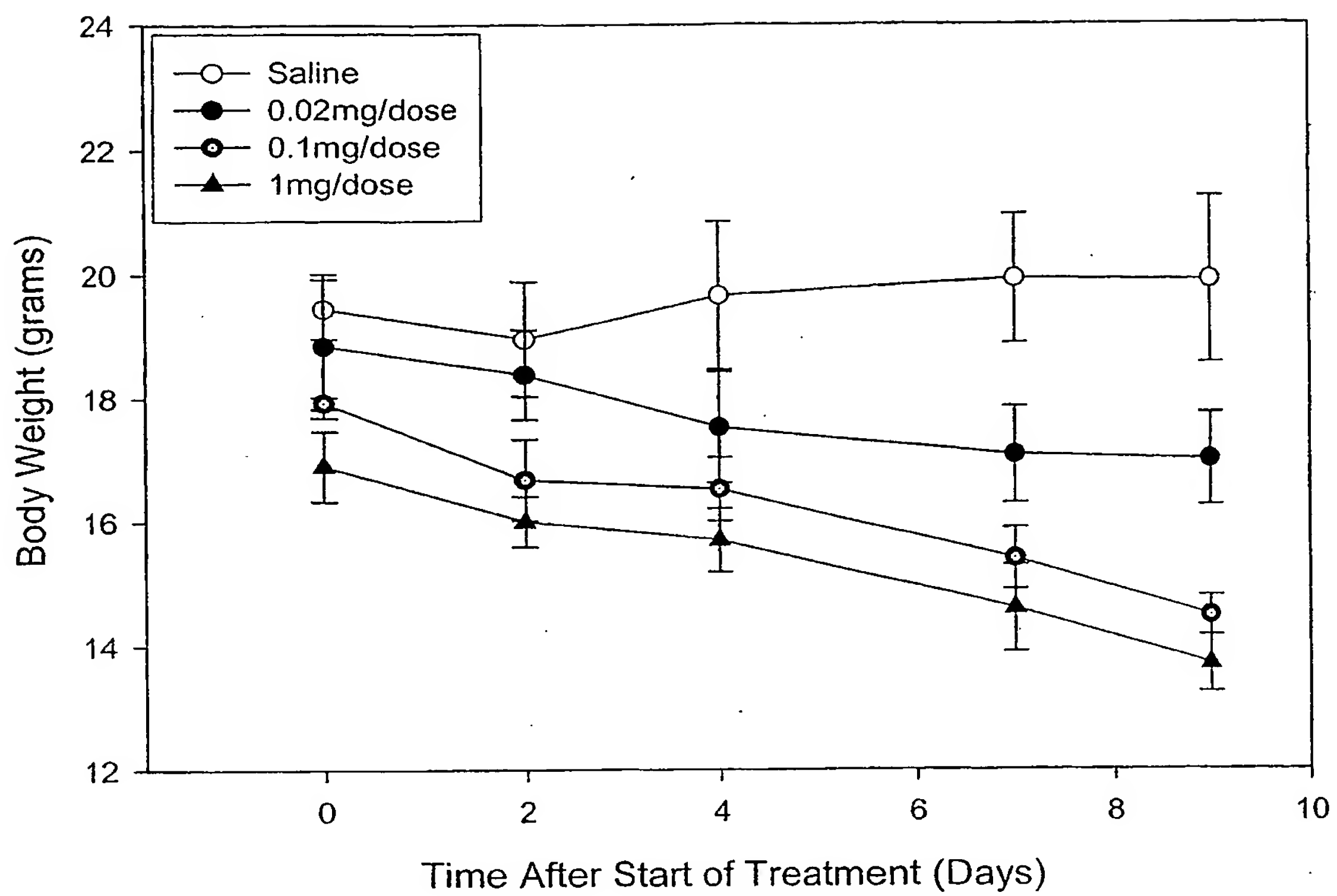


Fig. 17

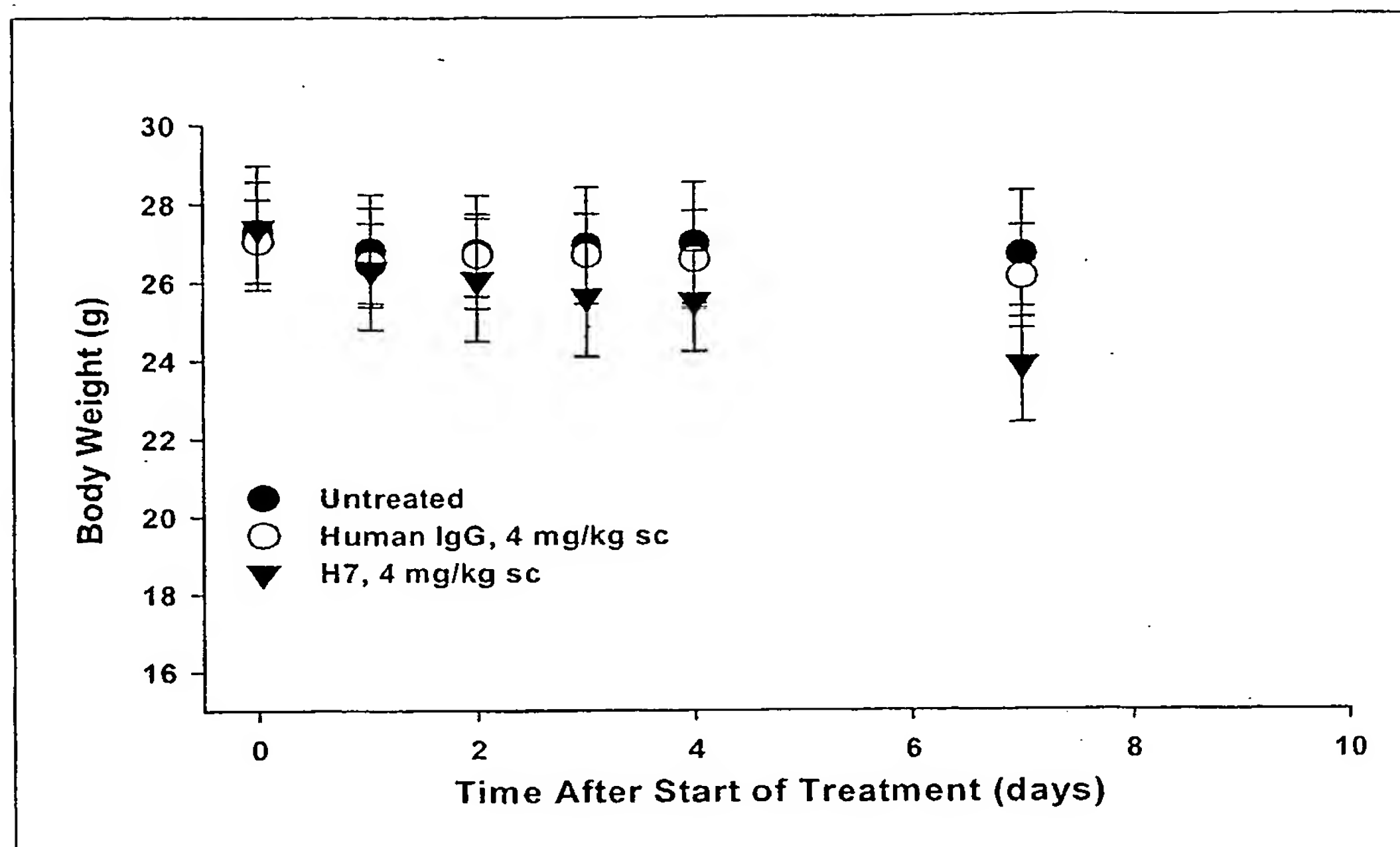


Fig. 18

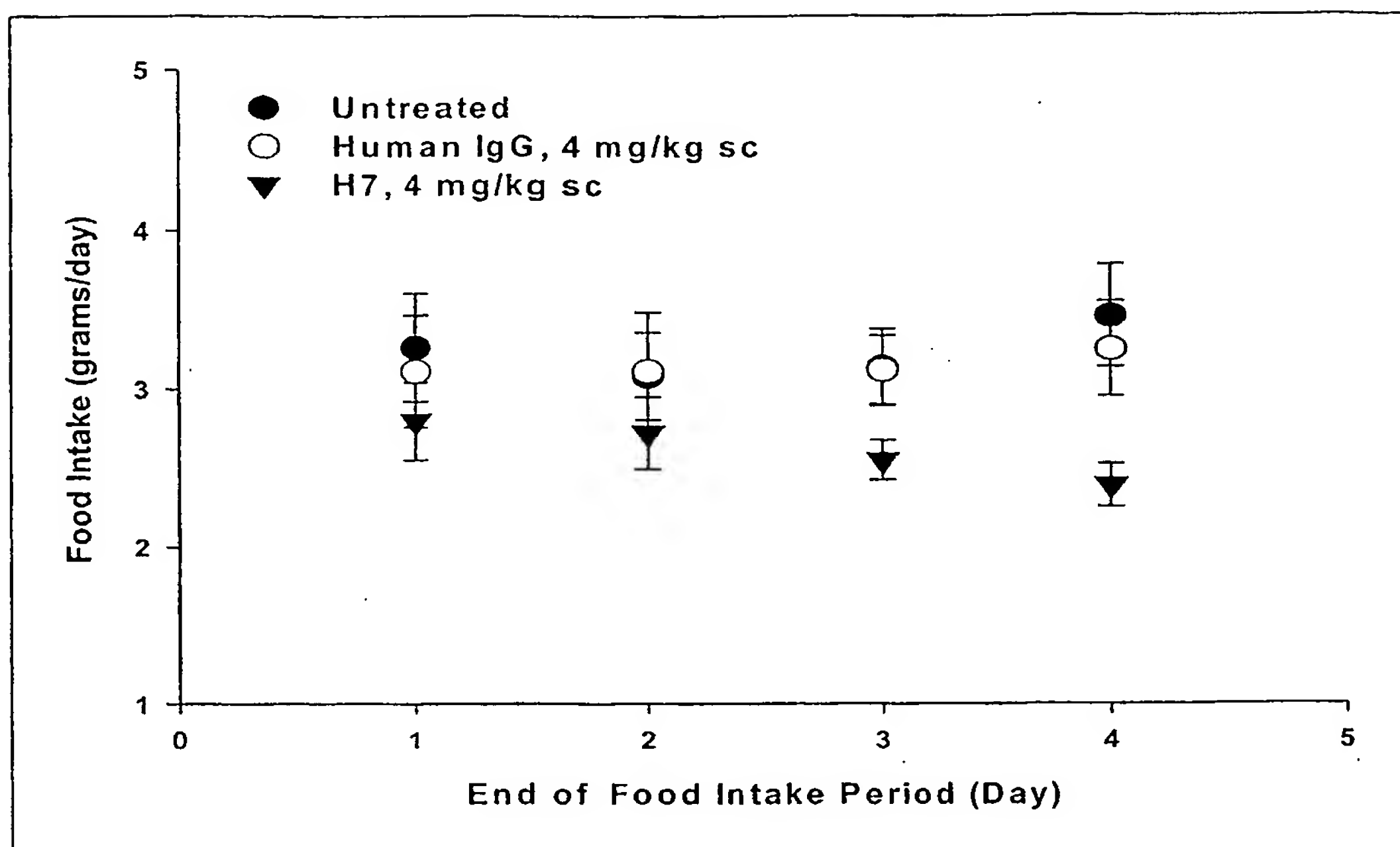


Fig. 19

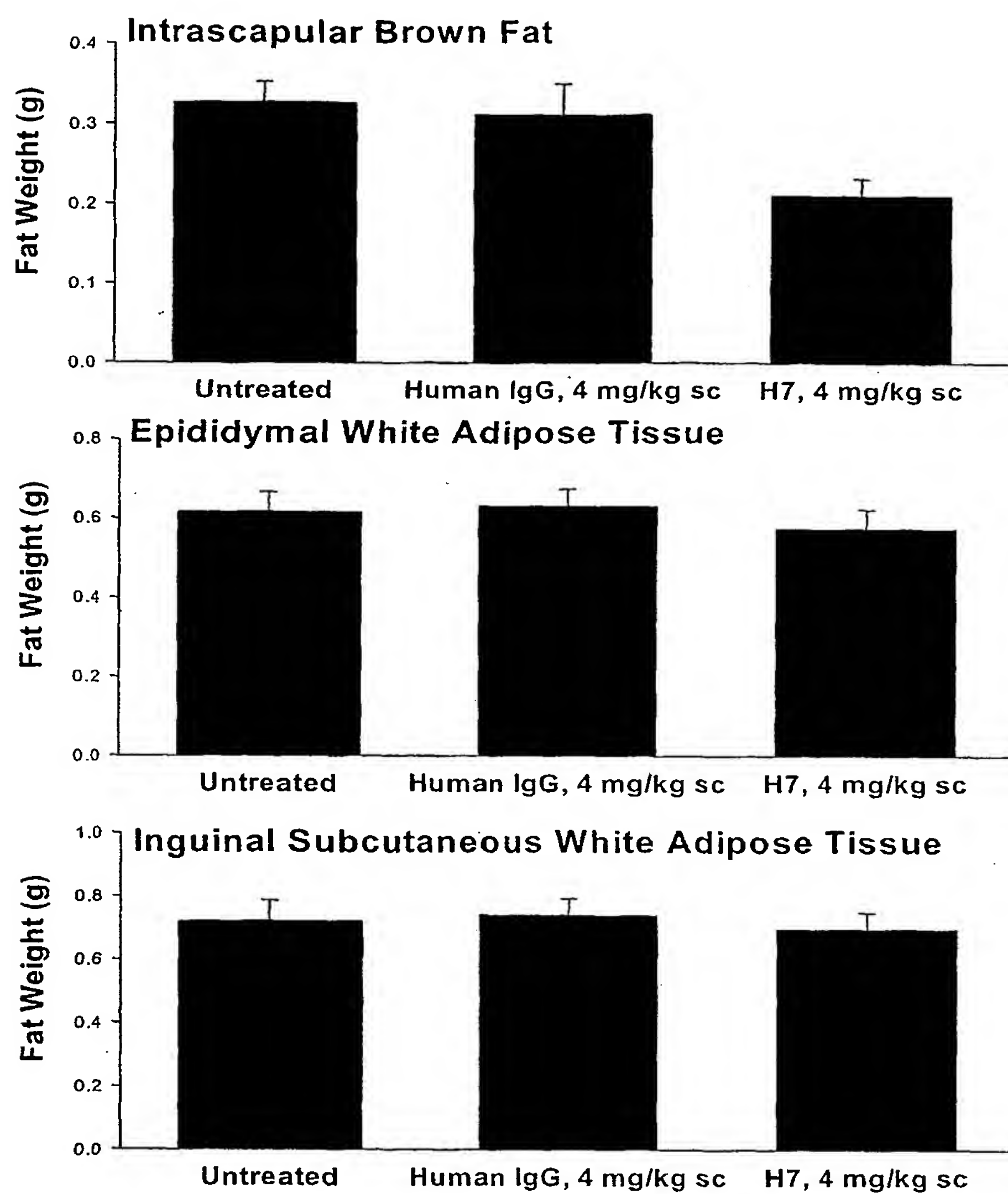


Fig. 20

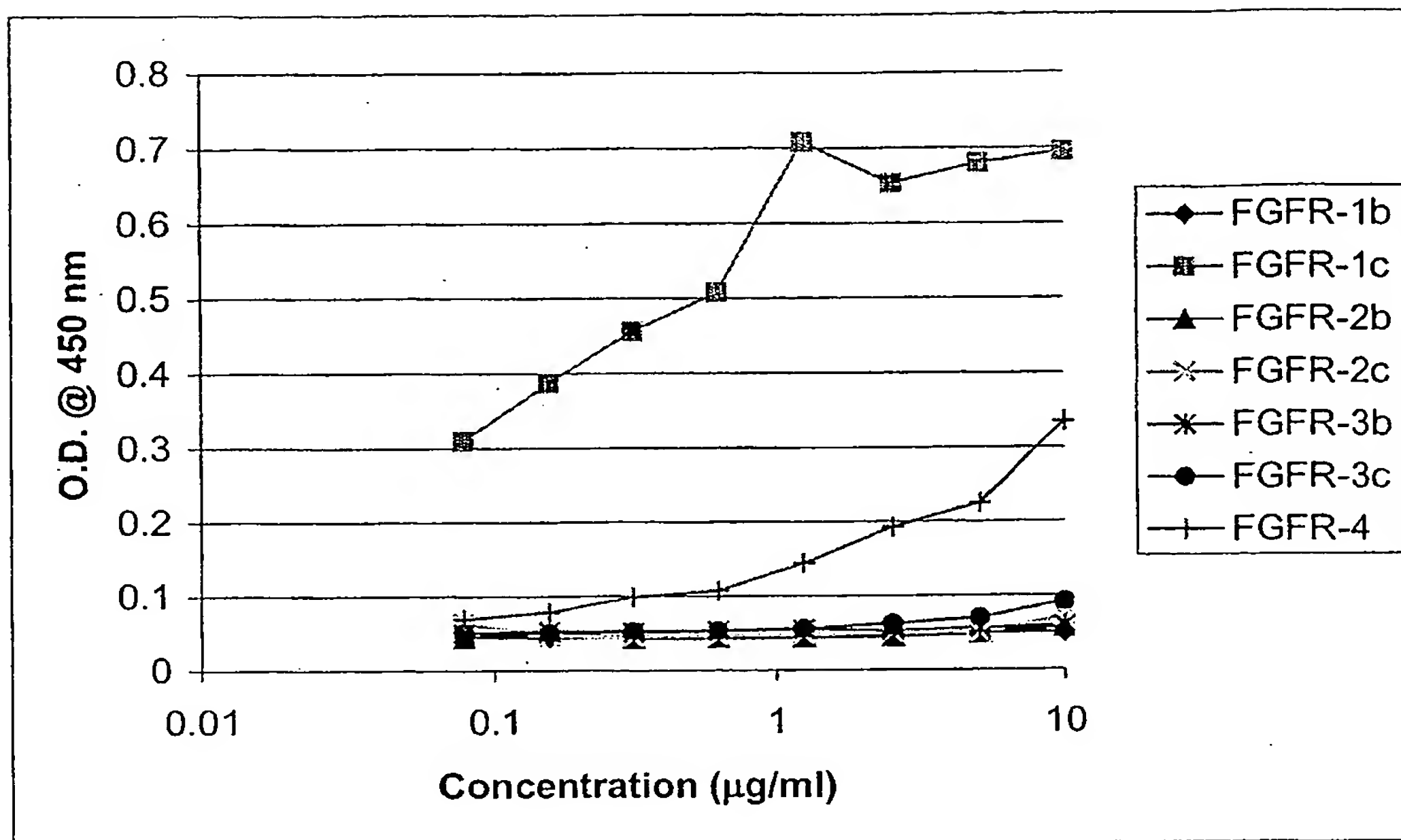


Fig. 21

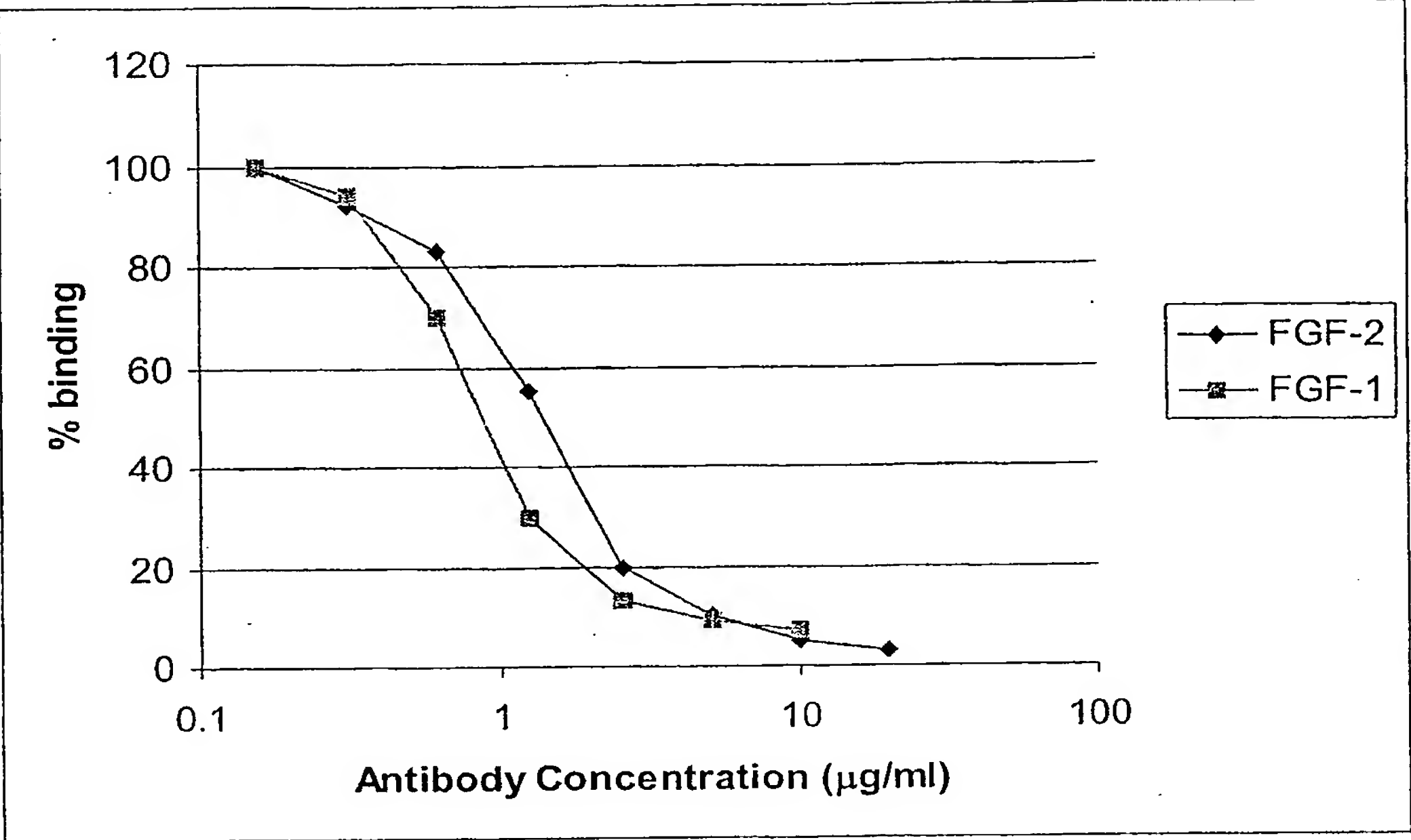


Fig. 22

FGF-2				
(ng/ml)	50	50	-	-
FR1-A1				
(μg/ml)	-	10	10	-

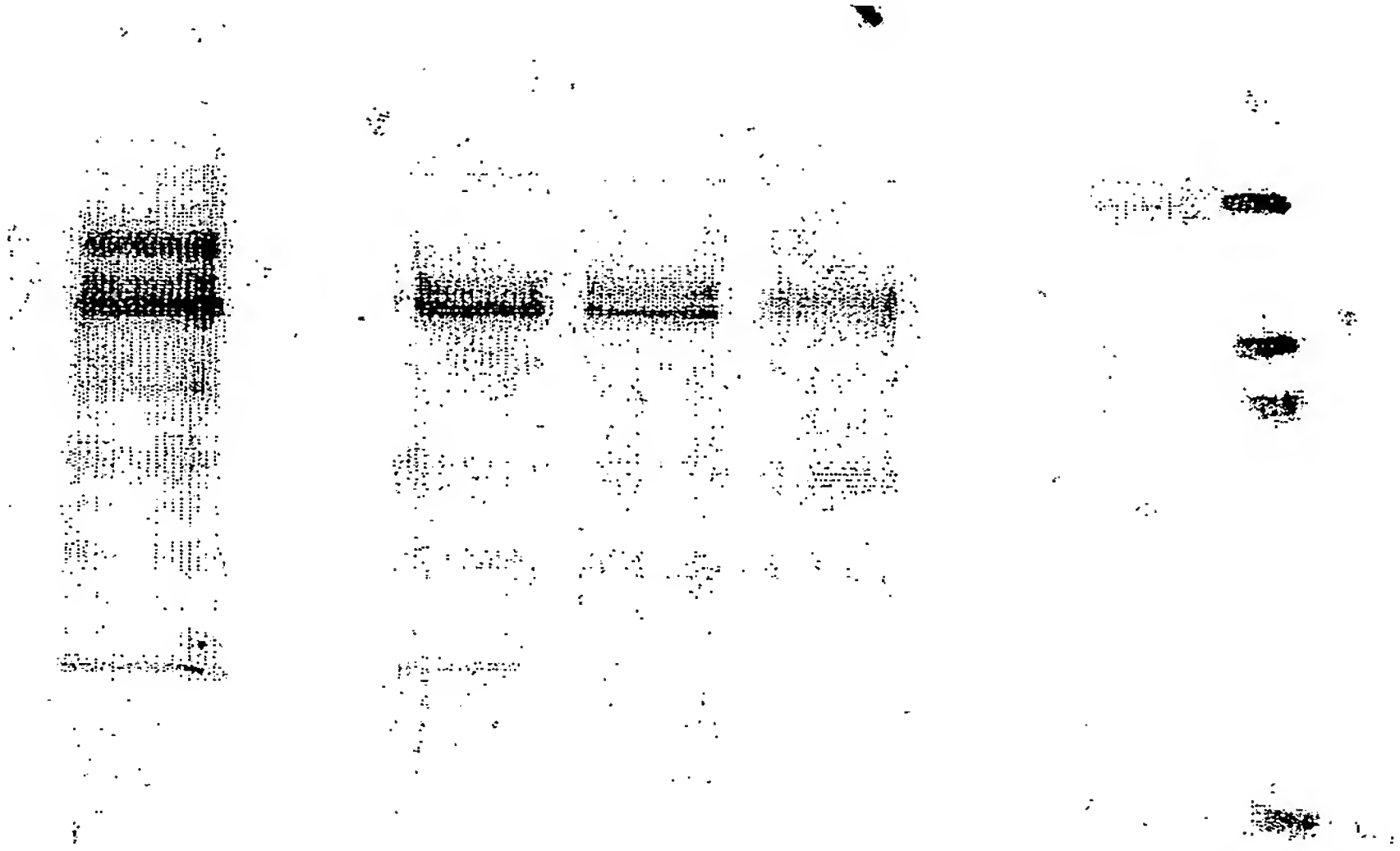


Fig. 23

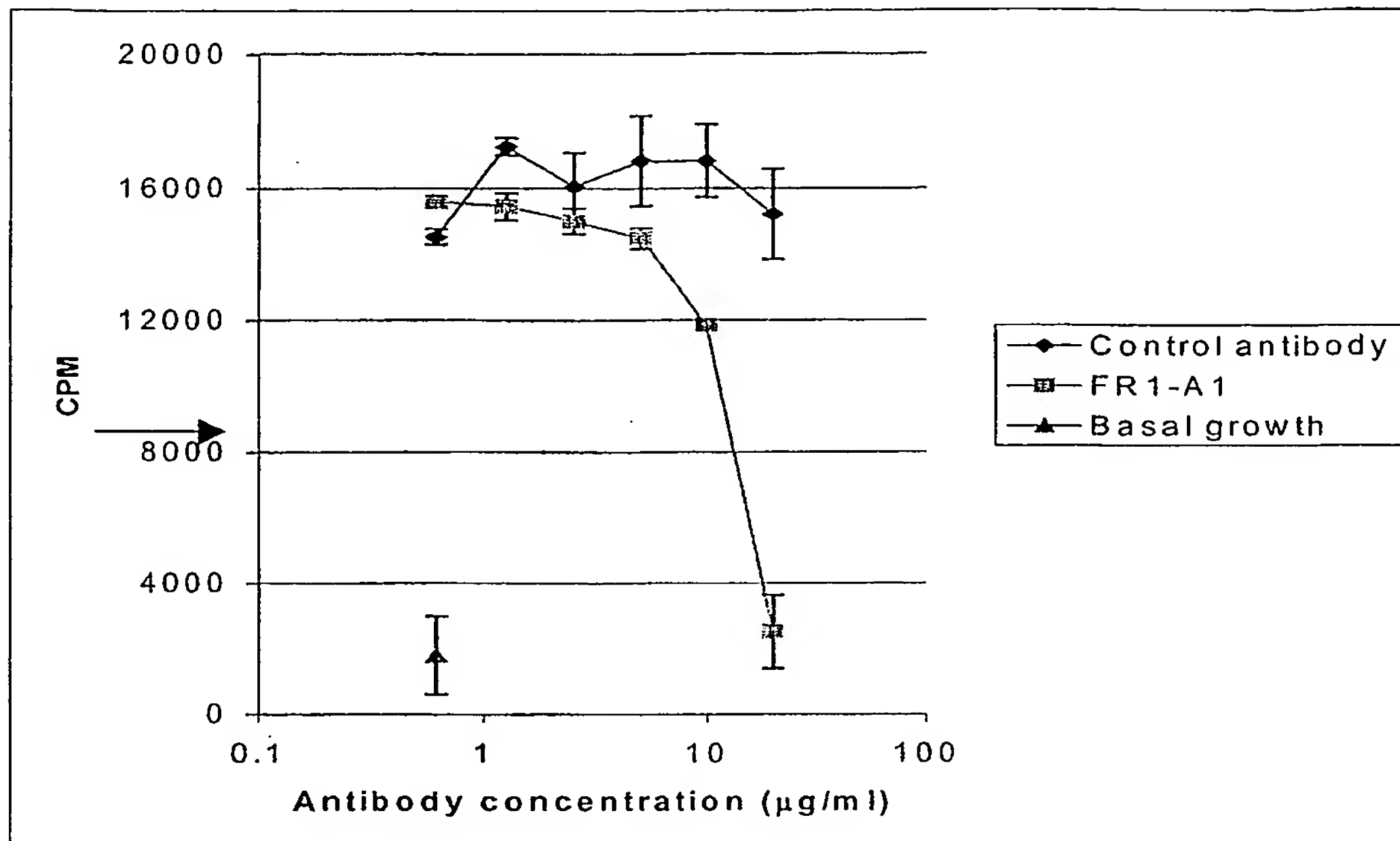


Fig. 24

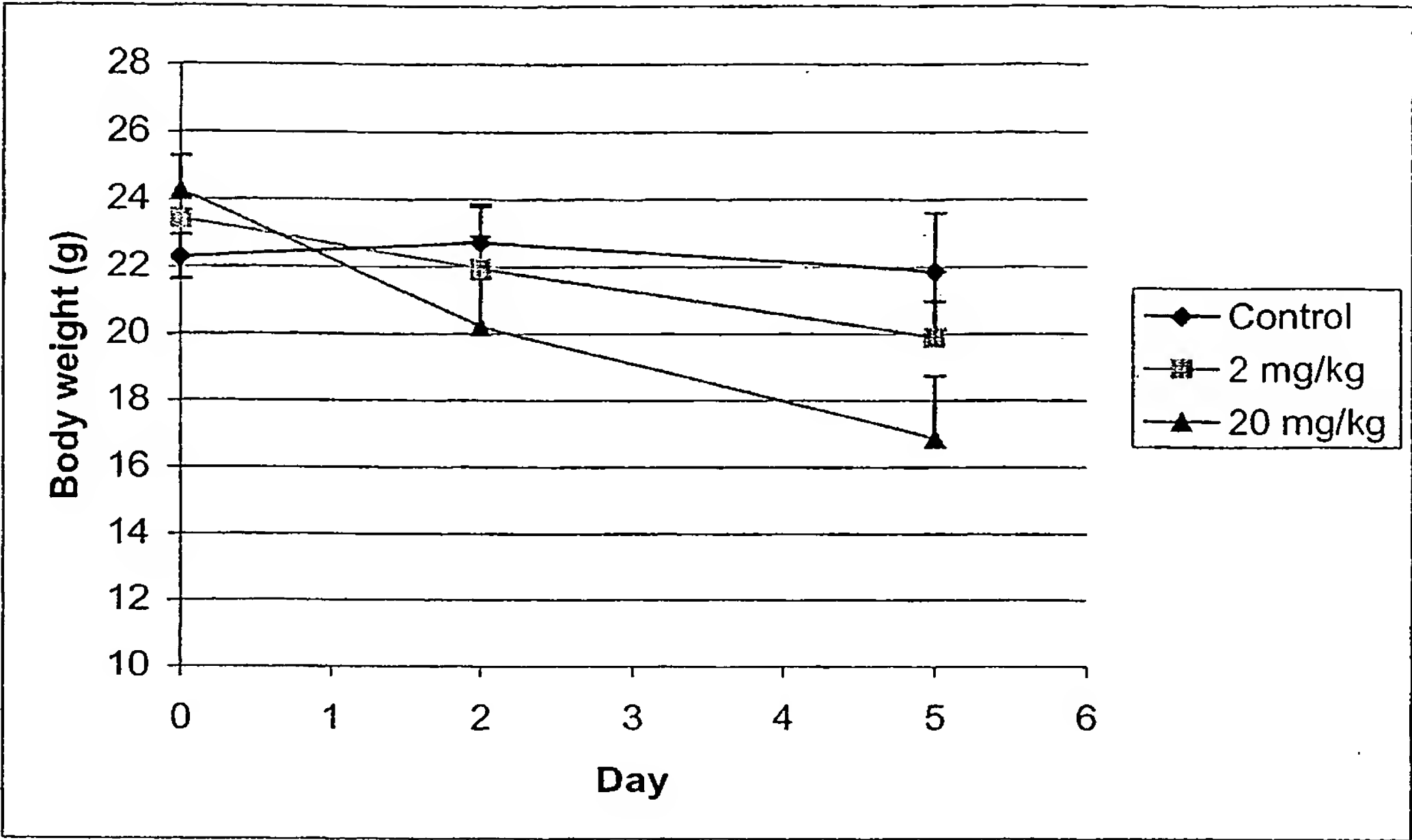


Fig .25

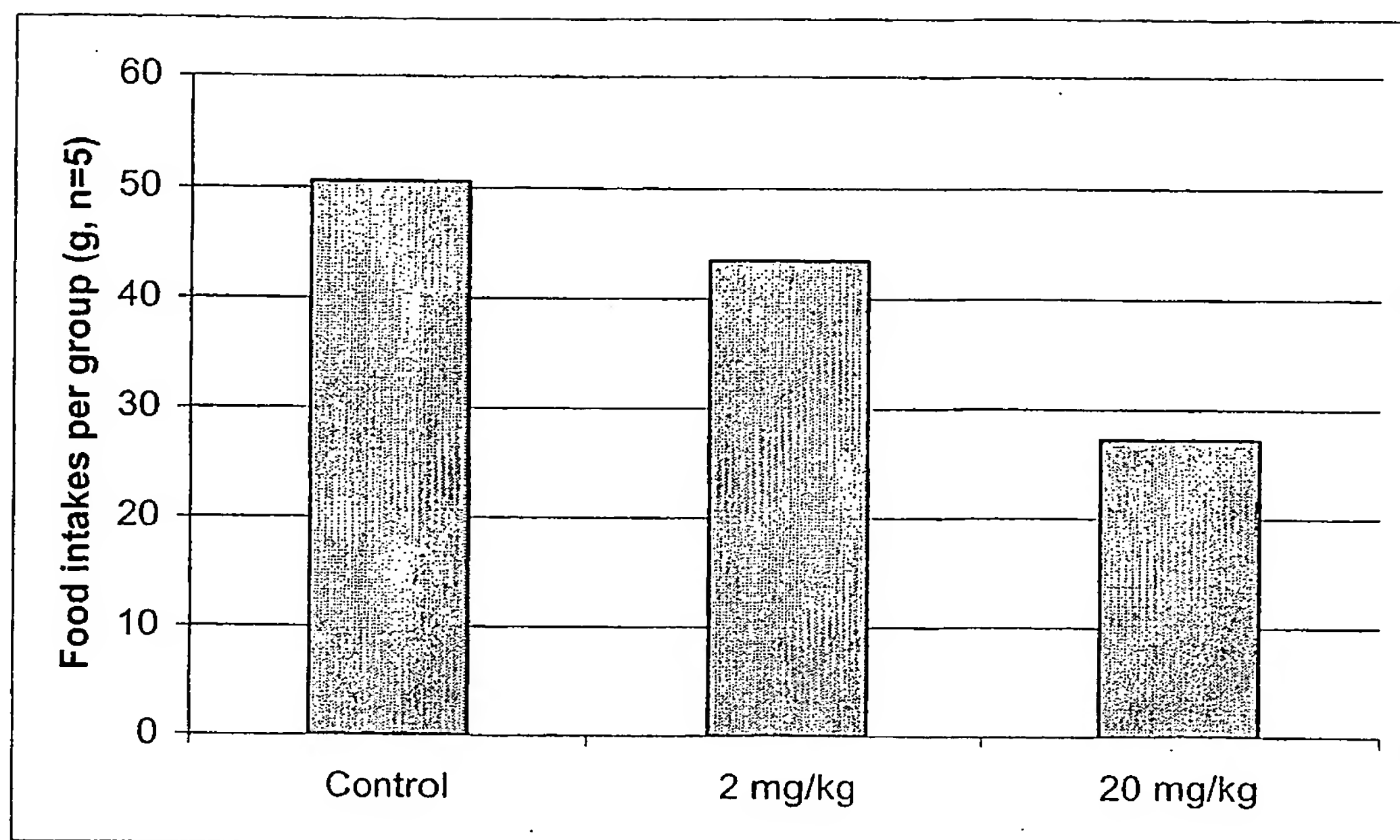


Fig. 26A

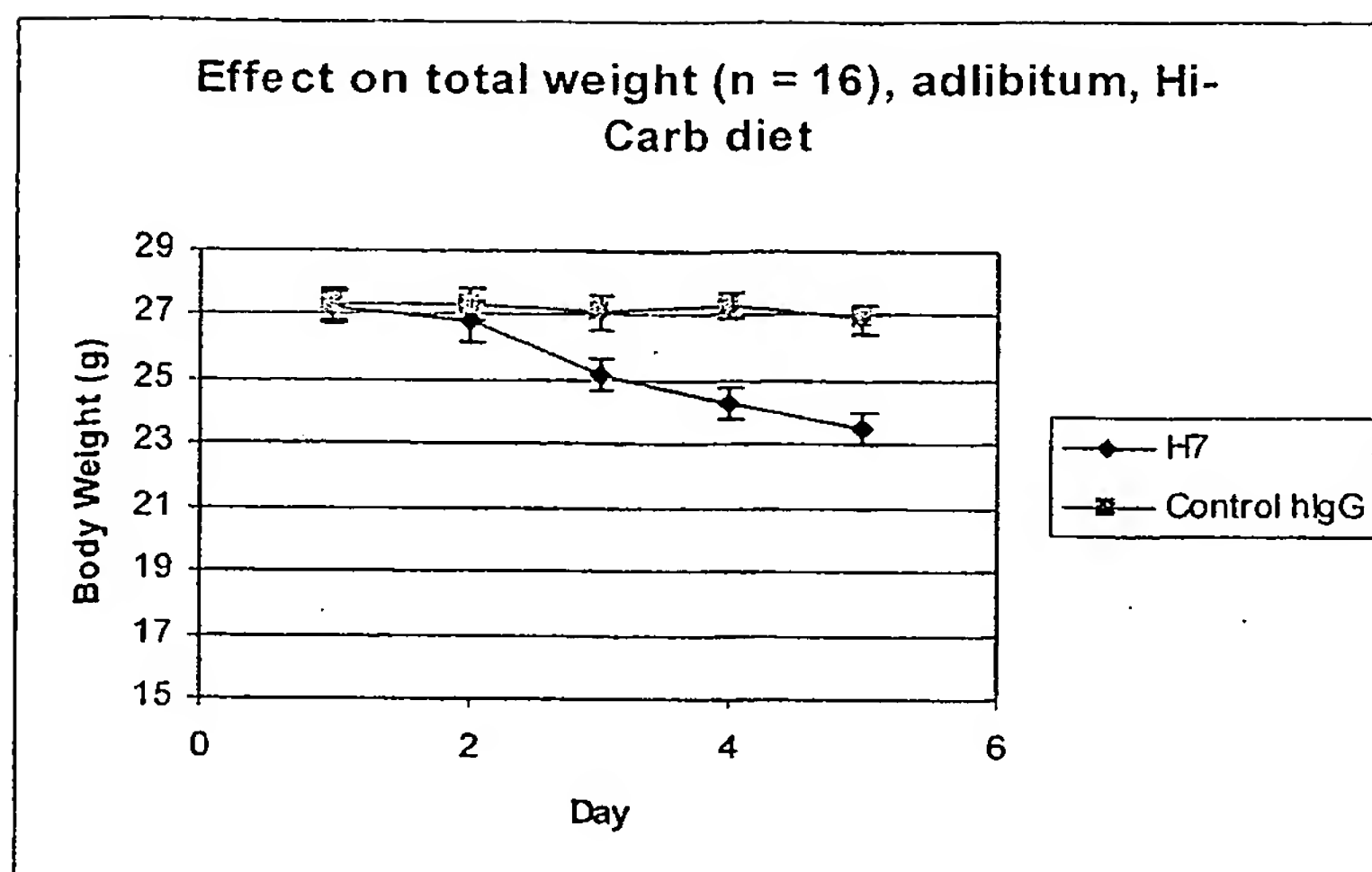


Fig. 26B

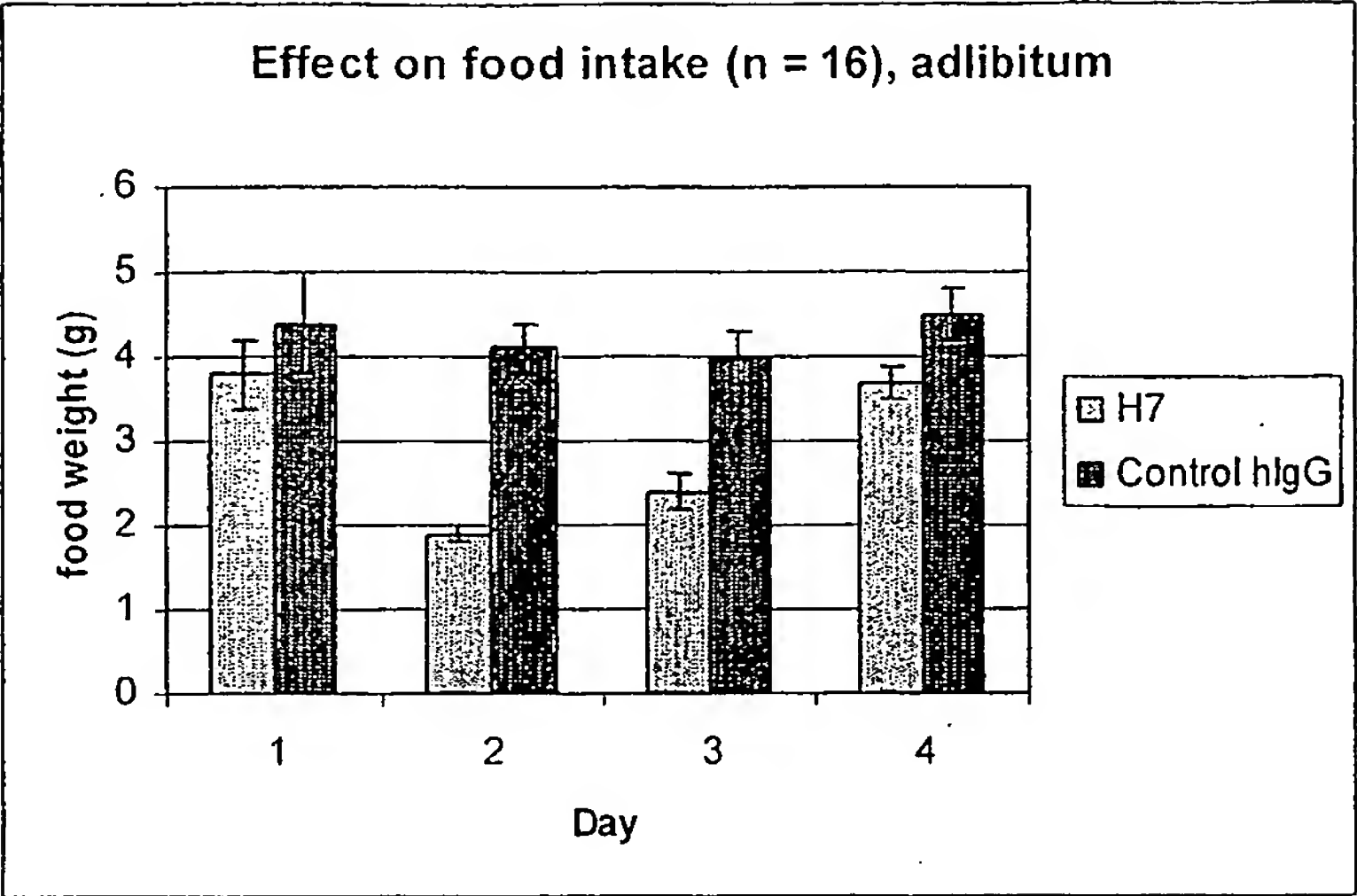


Fig 26C

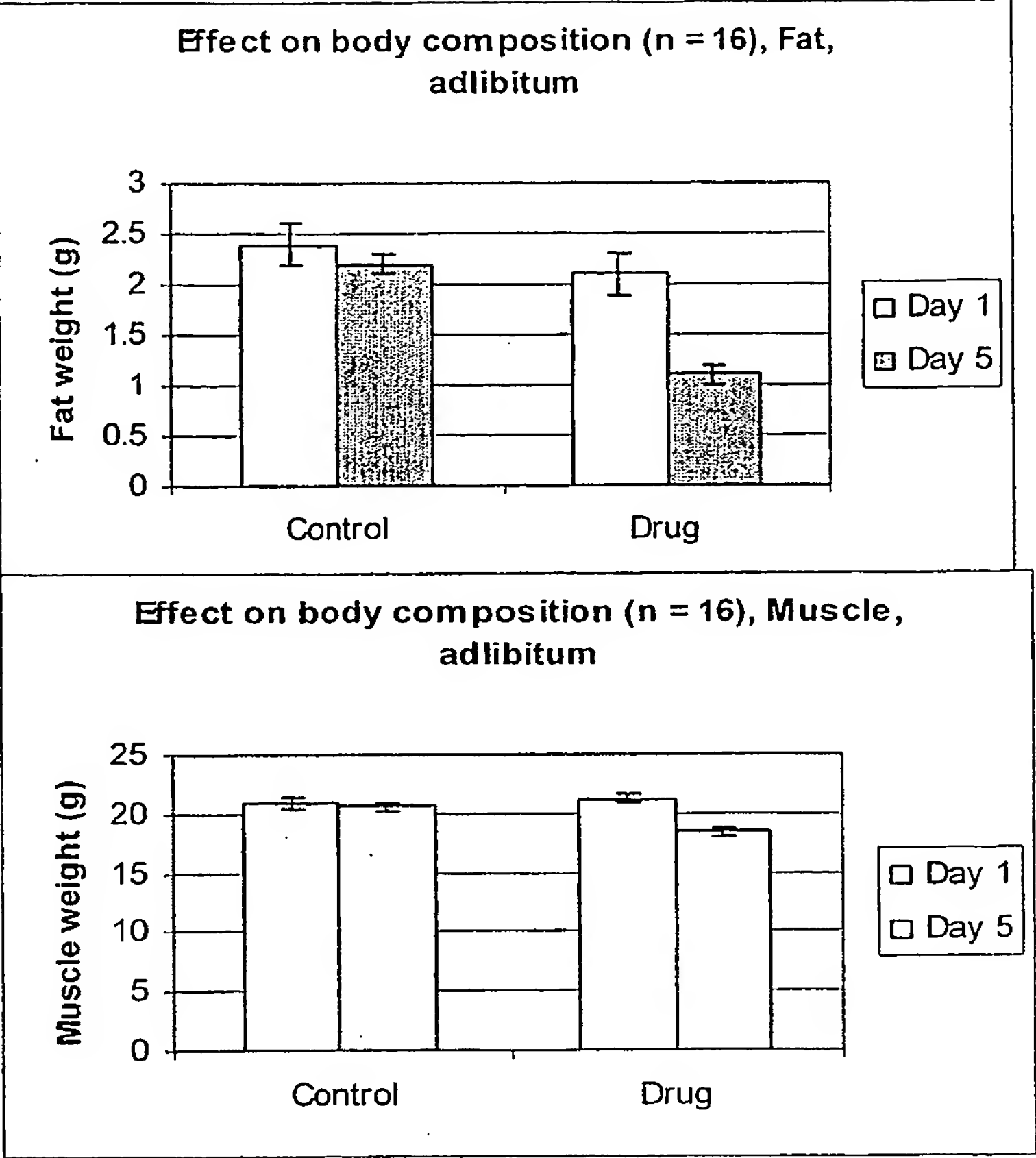


Fig. 26D

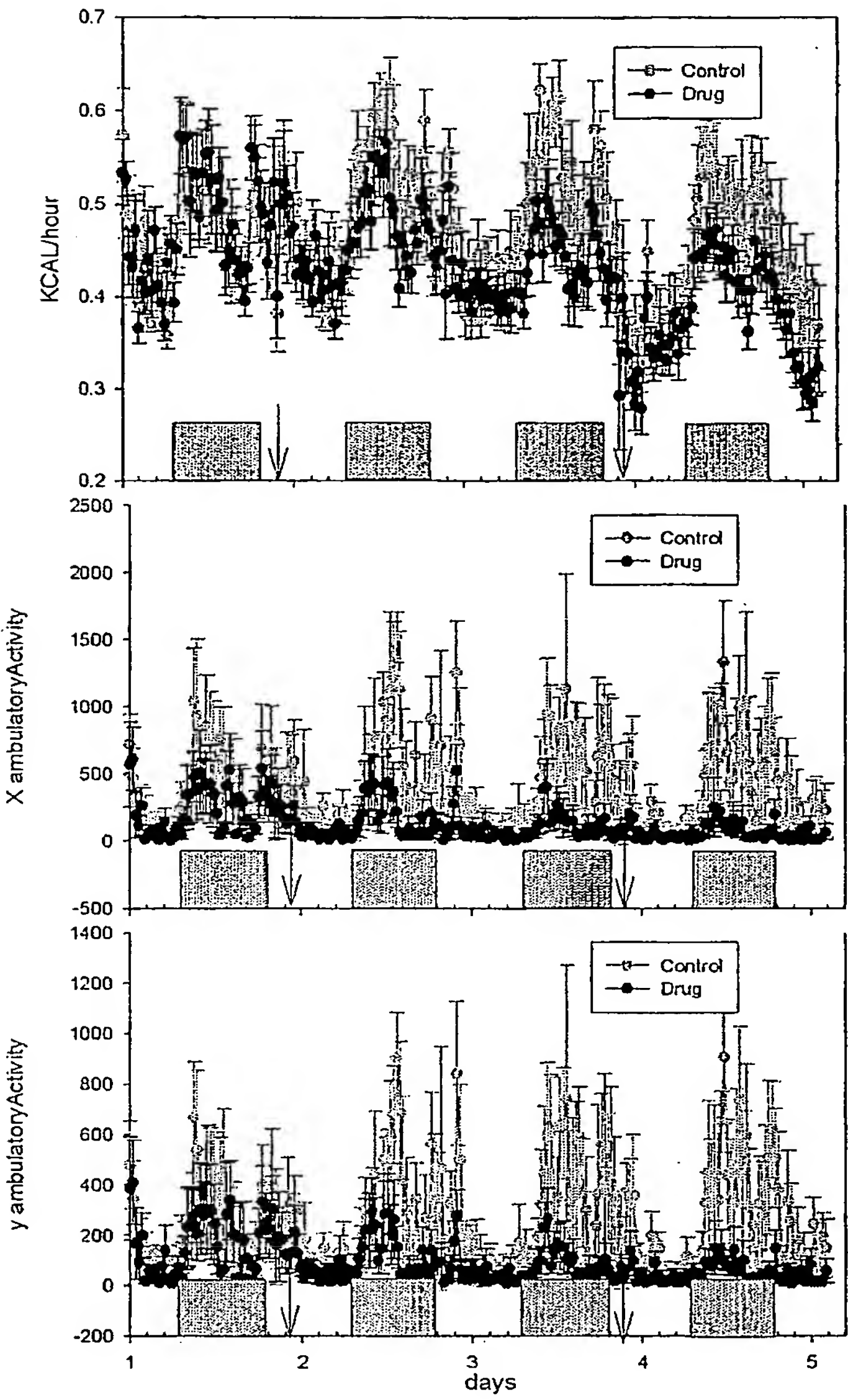


Fig. 26E

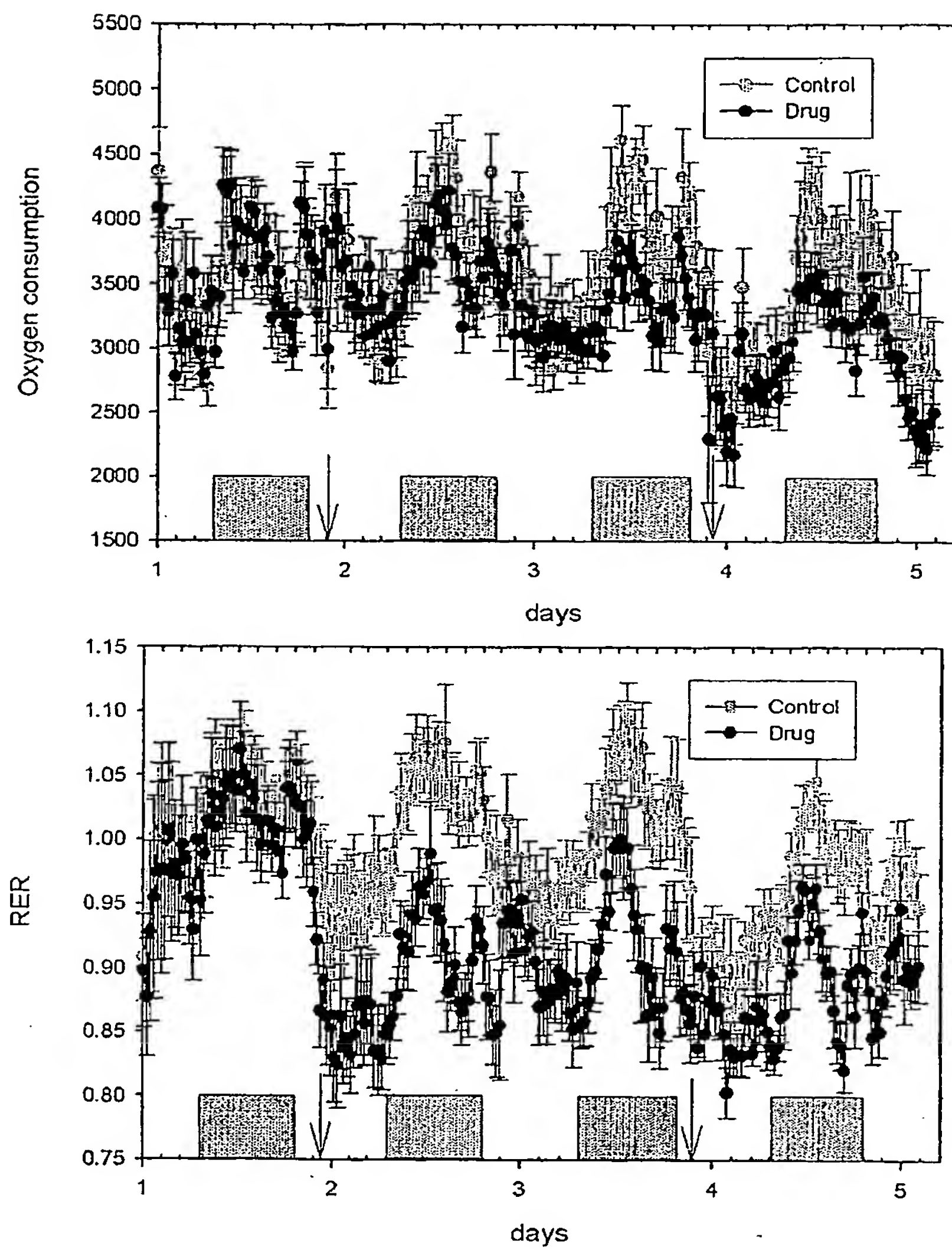


Fig. 27A

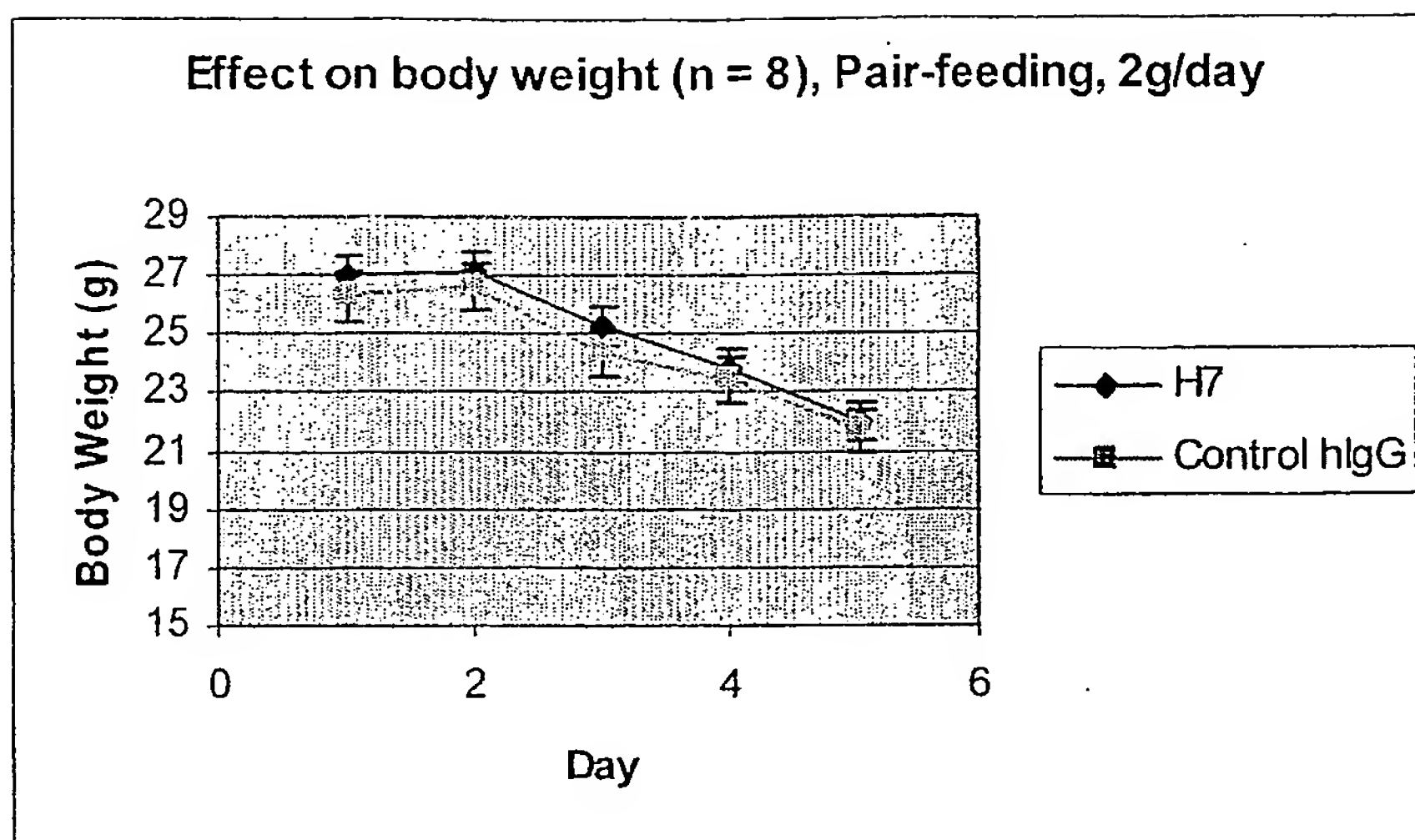


Fig. 27B

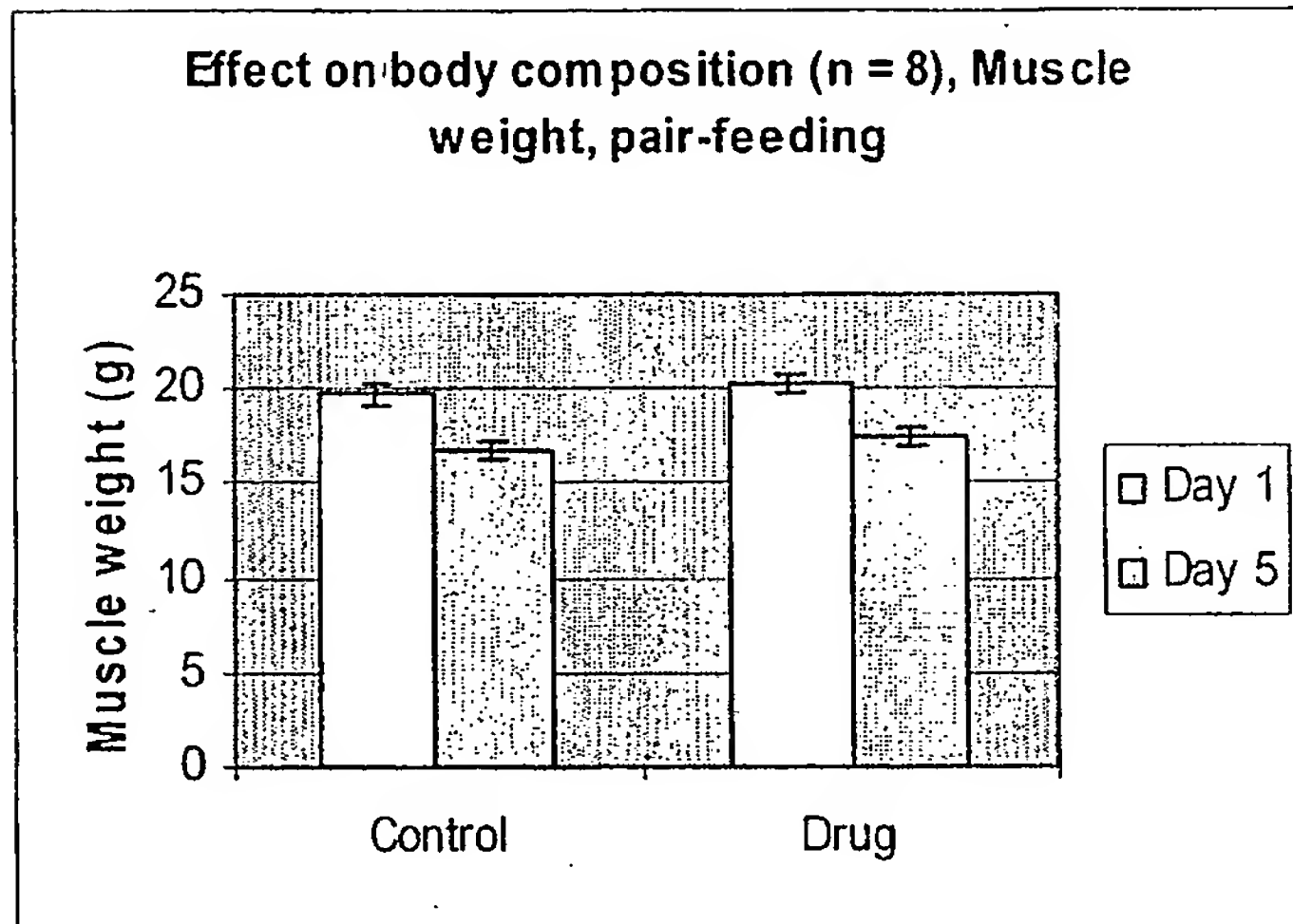
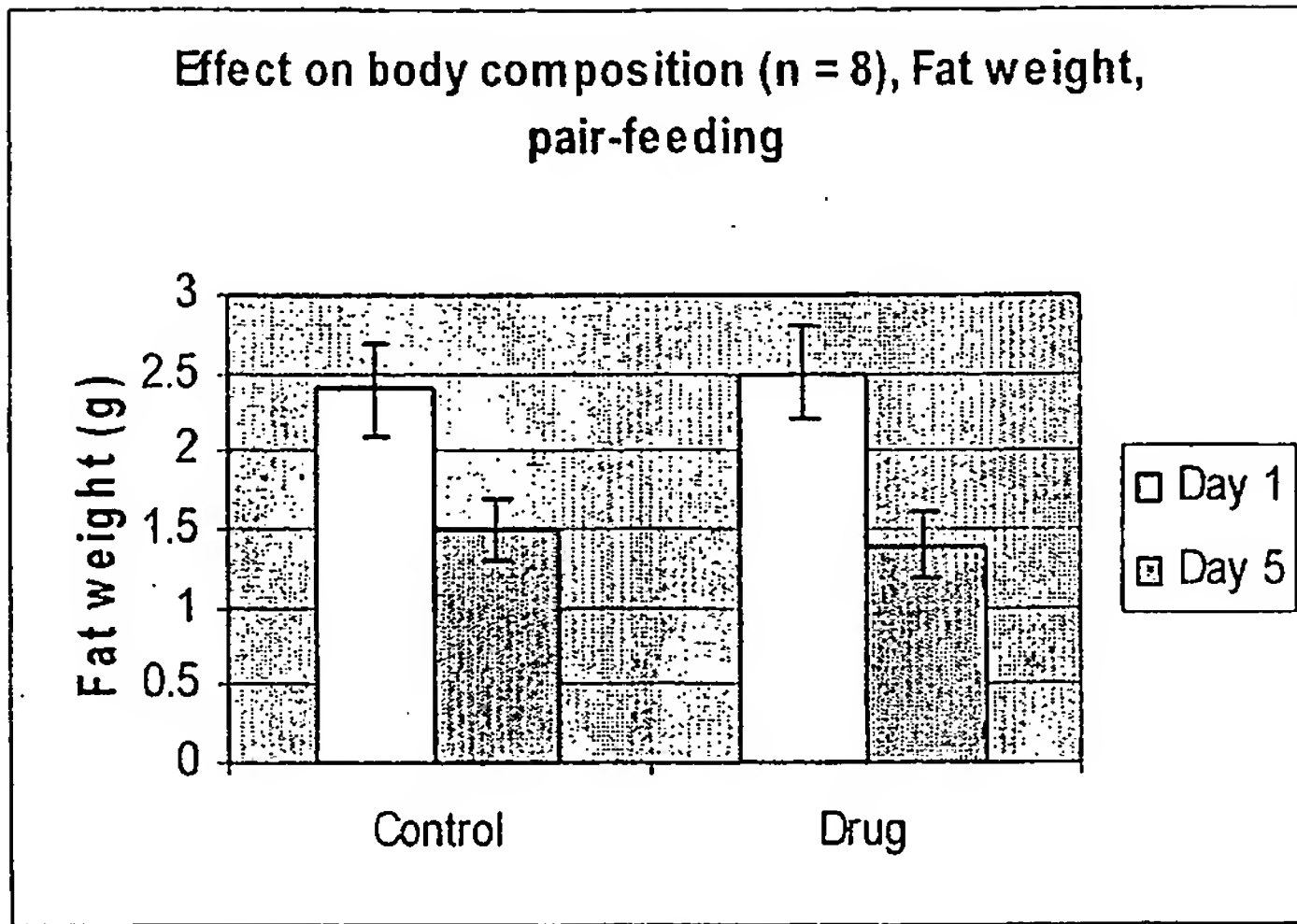


Fig. 27C

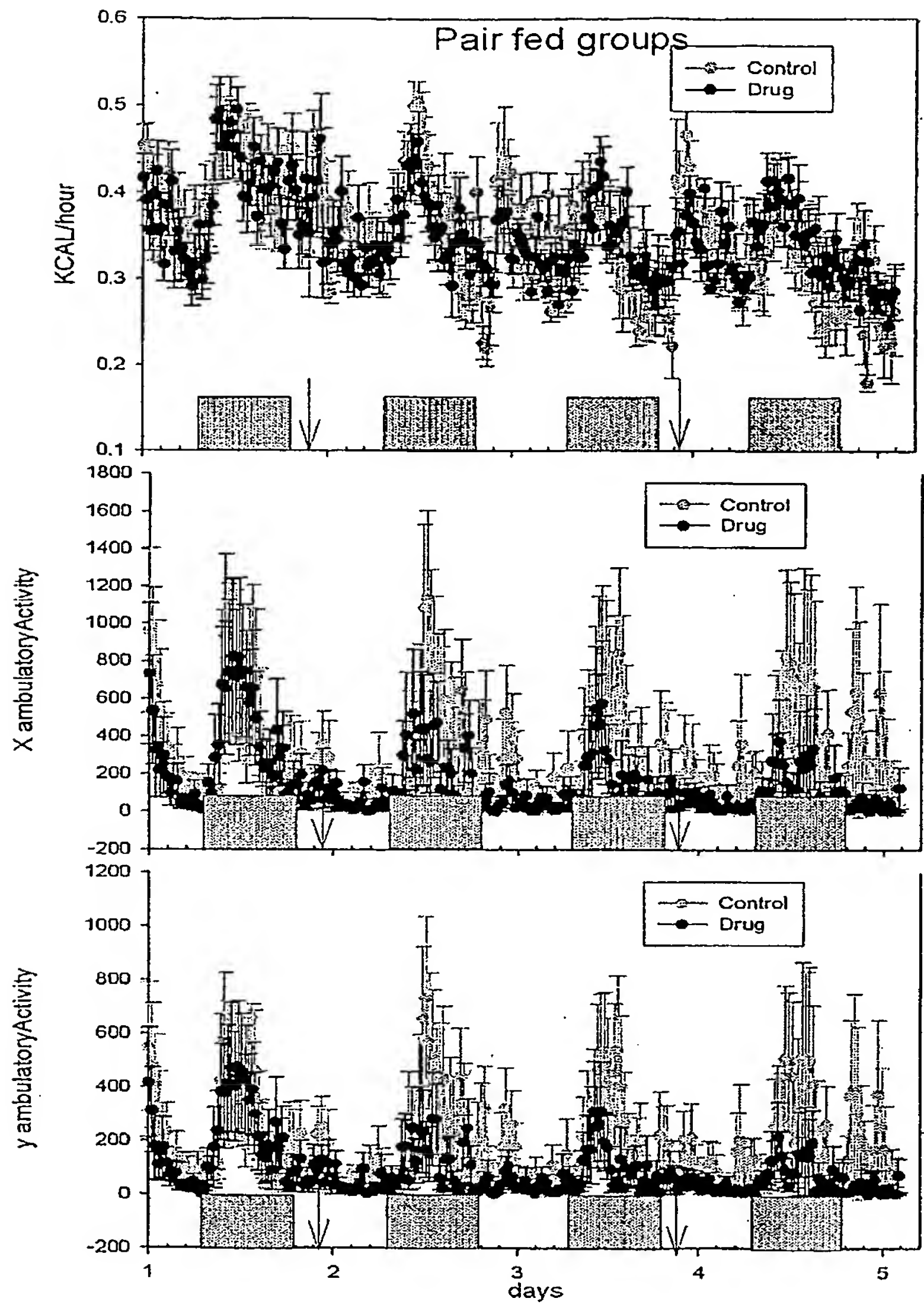


Fig. 27D

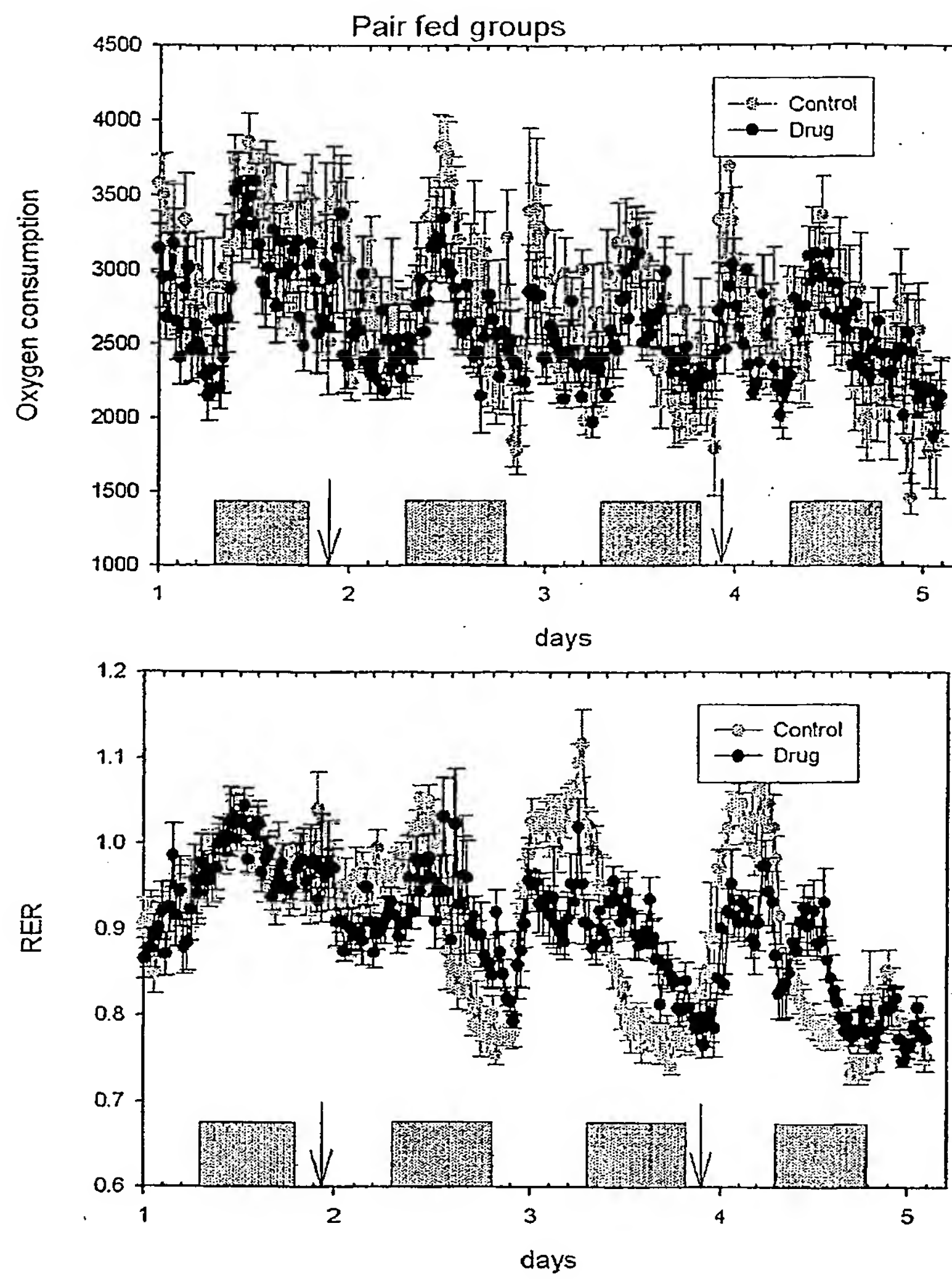


Fig. 28A. FR1-4H antibody variable sequences

Heavy chain variable region sequence (cDNA)
(gamma heavy chain)

CAGGTGCAGCTGGTGGAGTTTGGCCCAGGACTGGTGAAGCCTTCGGAGAC	50
CCTGTCCCTCACCTGCACTGTCTCTGGTGGCTCCATCAGTAGTTACTACT	100
GGAGCTGGATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGATTGGGTAT	150
ATCTATTACAGTGGGAGCACCAACTACAACCCCTCCCTCAAGAGTCGAGT	200
CGCCATATCAGTAGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCT	250
CTGTGACCGCCGCGGACACGGCCGTGTATTACTGTGCGAGAGAGTATTAC	300
TATGATAGTAGTGGTTATTACTTTTATGCTTTTGATATCTGGGGCCAAGG	350
GACCACGGTCACCGTCTCAAGC	372

Heavy chain variable region sequence (amino acid)

QVQLVEFGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGY	50
IYYSGSTNYPNPSLKSRLVAISVDTSKNQFSLKLSSVTAADTAVYYCAREYY	100
YDSSGYFYAFDIWGQGTITVTVSS	124

Light chain variable region sequence (cDNA)

CTGCCTGTGCTGACTCAGCCCCCTCAGCGTCTGGGACCCCCGGGCAGAG	50
GGTCTCCATCTCTTGTTCTGGAAGCAGCTCCAACATCGGAAGTAATTATG	100
TATACTGGTACCAGCAGCTCCCAGGAACGGCCCCCAAACCTCCTCATCTTT	150
AGGAATAATCAGCGGCCCTCAGGGGTCCCTGACCGATTCTCTGGCTCCAA	200
GTCTGGCACTTCAGCCTCCCTGGCCATCAGTGGGCTCCGGTCCGAGGATG	250
AGGCTGATTATTACTGTGCAGCATGGGATGACAGCCTGAGTGGTTGGGTG	300
TTCGGCGGAGGGACCAAGCTGACCGTCCTAGGT	333

Light chain variable region sequence (amino acid).
(Lambda light chain)

LPVLTQPPSASGTPGQRVSISSGSSSNIGSNYVYWYQQLPGTAPKLLIF	50
RNNQRPSGVPDRFSGSKSGTSASLAISGLRSEDEADYYCAAWDDSLSGWV	100
FGGGTKLTVLG	111

Fig. 28B. FR1-4H antibody variable sequence CDRs

CDR amino acid sequences

 V_H :

CDR1	SYYWS
CDR2	YIYYSGSTNYPNPSLKS
CDR3	EYYDSSGYFYAFDI

 V_L :

CDR1	SGSSSNIGSNYVY
CDR2	RNNQRPS
CDR3	AAWDDSLSGWV

CDR nucleic acid sequences

 V_H :

CDR1	AGTTACTACTGGAGC
CDR2	TATATCTATTACAGTGGGAGCACCAACTACAACCCCTCCCTCAAGAGT
CDR3	GAGTATTACTATGATAGTAGTGGTTATTACTTTTATGCTTTTGATATC

 V_L :

CDR1	TCTGGAAGCAGCTCCAACATCGGAAGTAATTATGTATAC
CDR2	AGGAATAATCAGCGGCCCTCA
CDR3	GCAGCATGGGATGACAGCCTGAGTGGTTGGGTG

Fig. 29

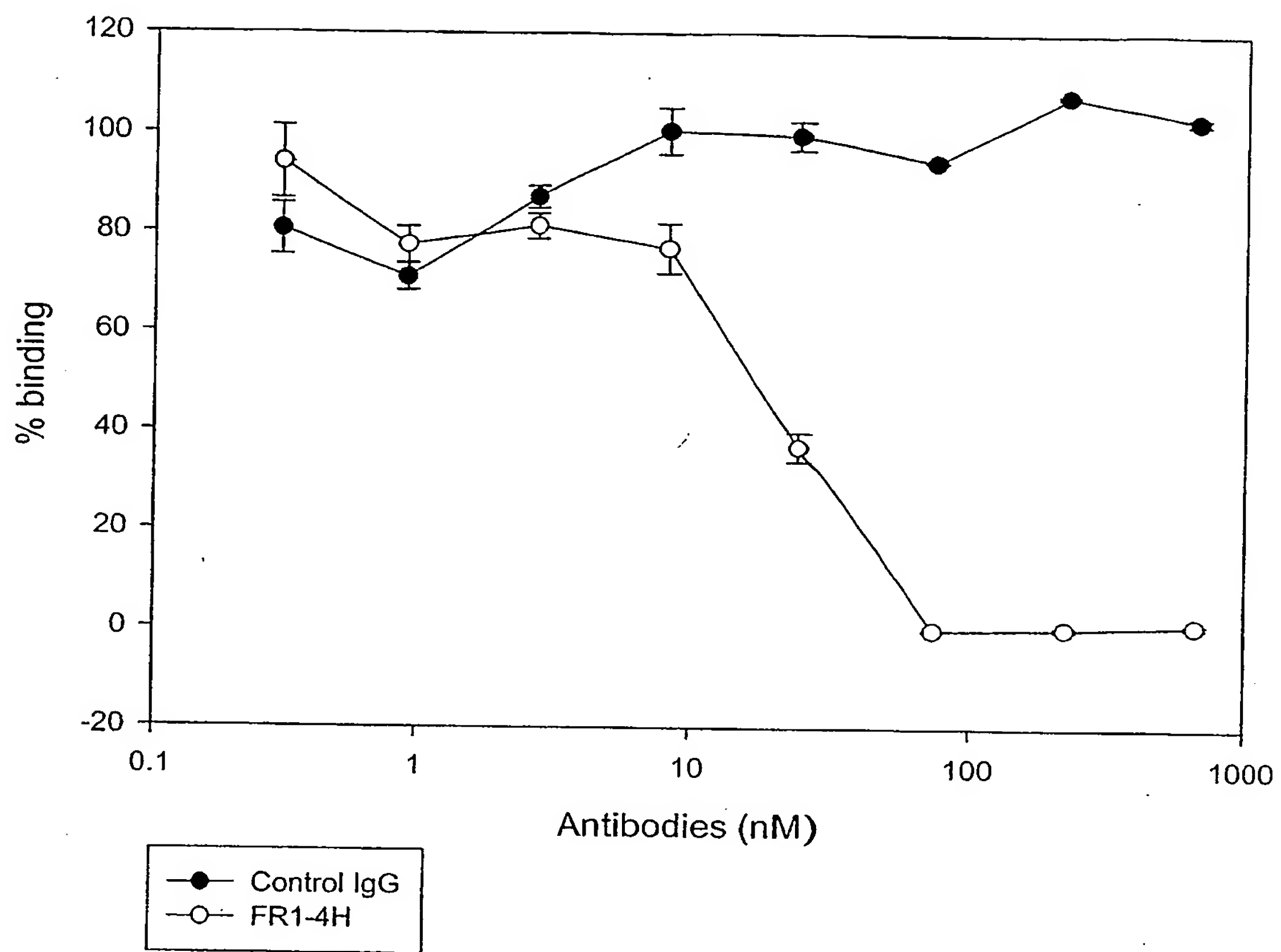
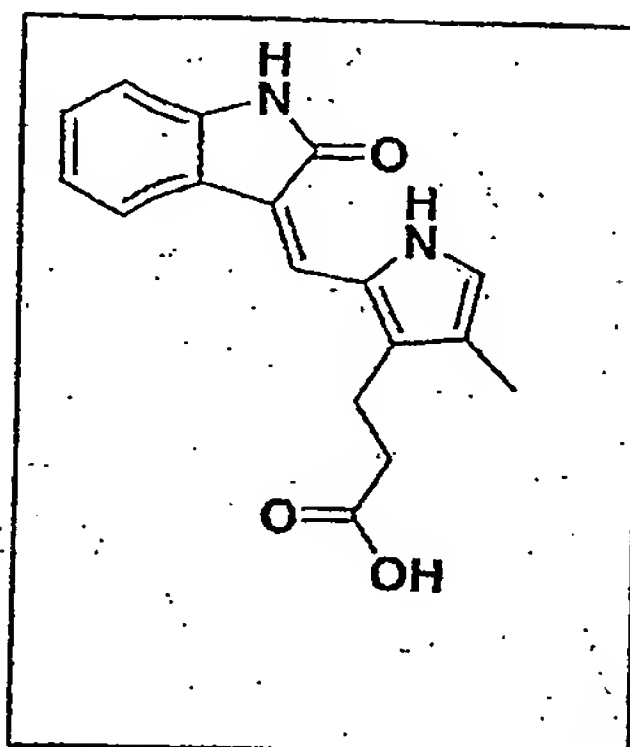
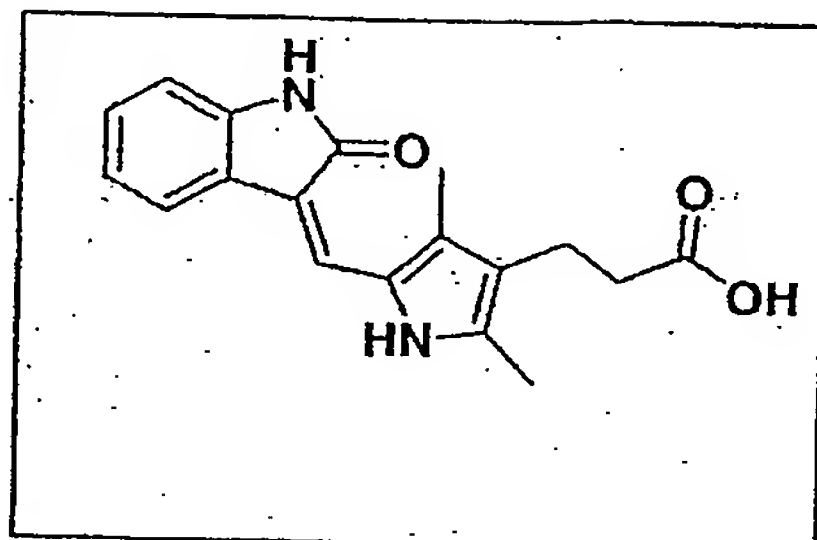
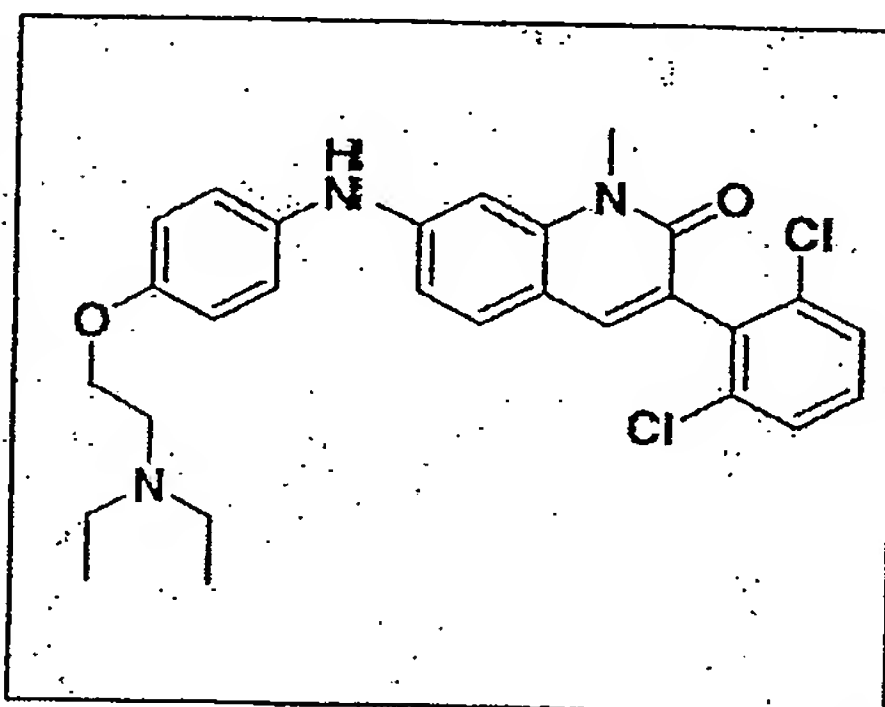
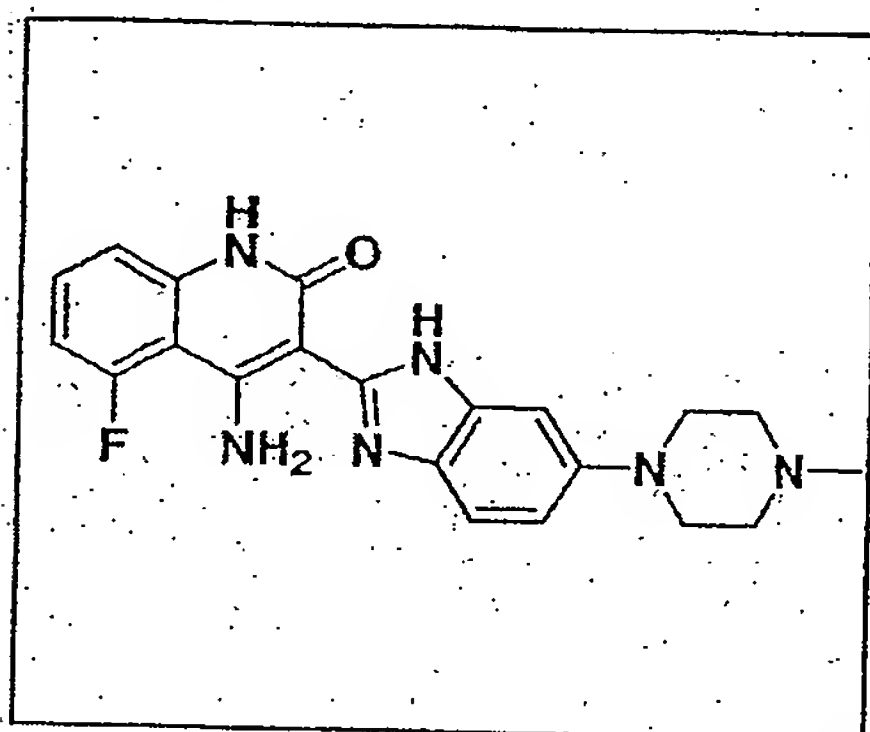


Fig. 30. Examples of FGFR small molecule inhibitors.

Indolinone derivatives:



Quinolinone derivatives:



Pyrimido-pyridine derivatives:

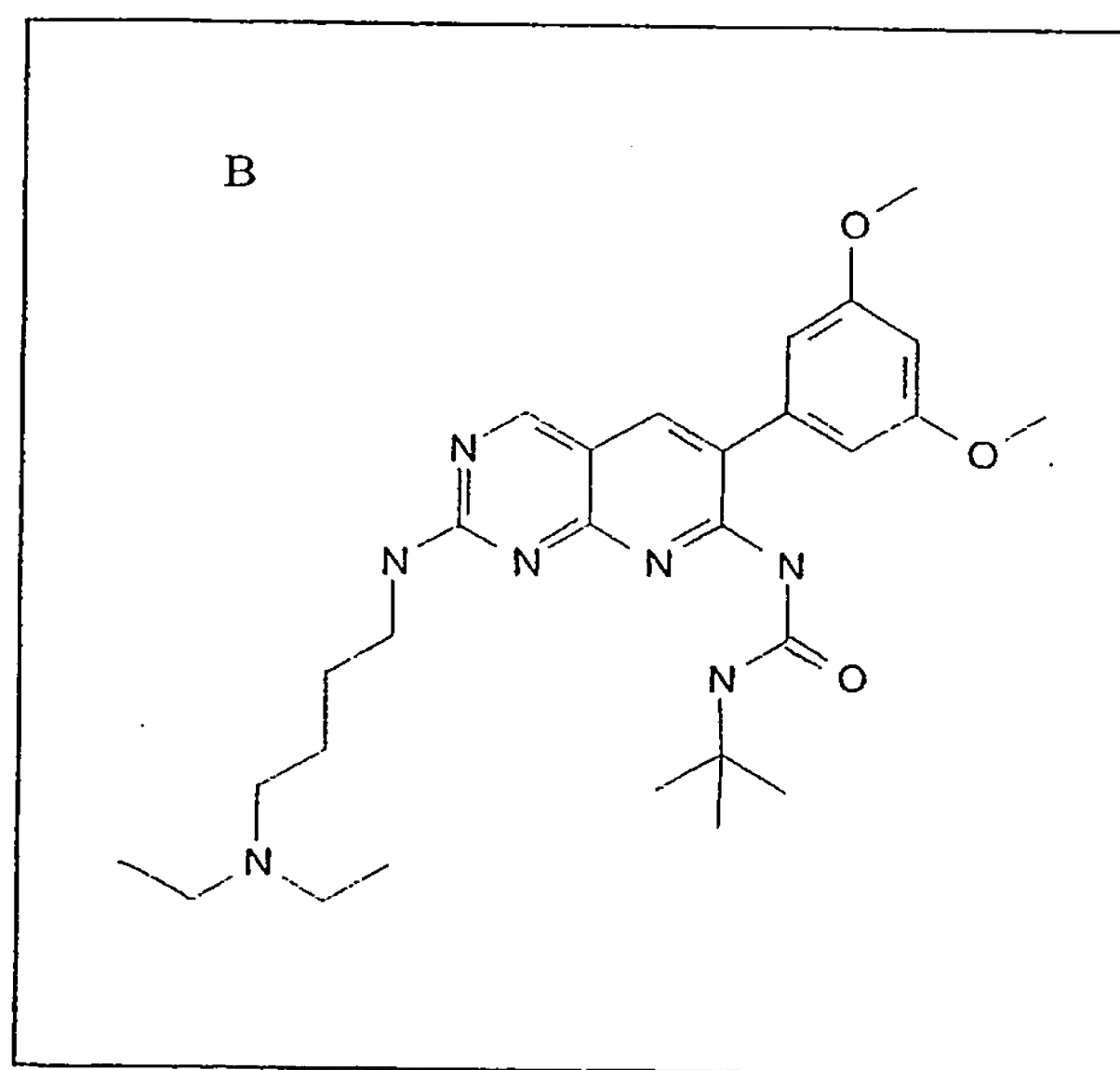
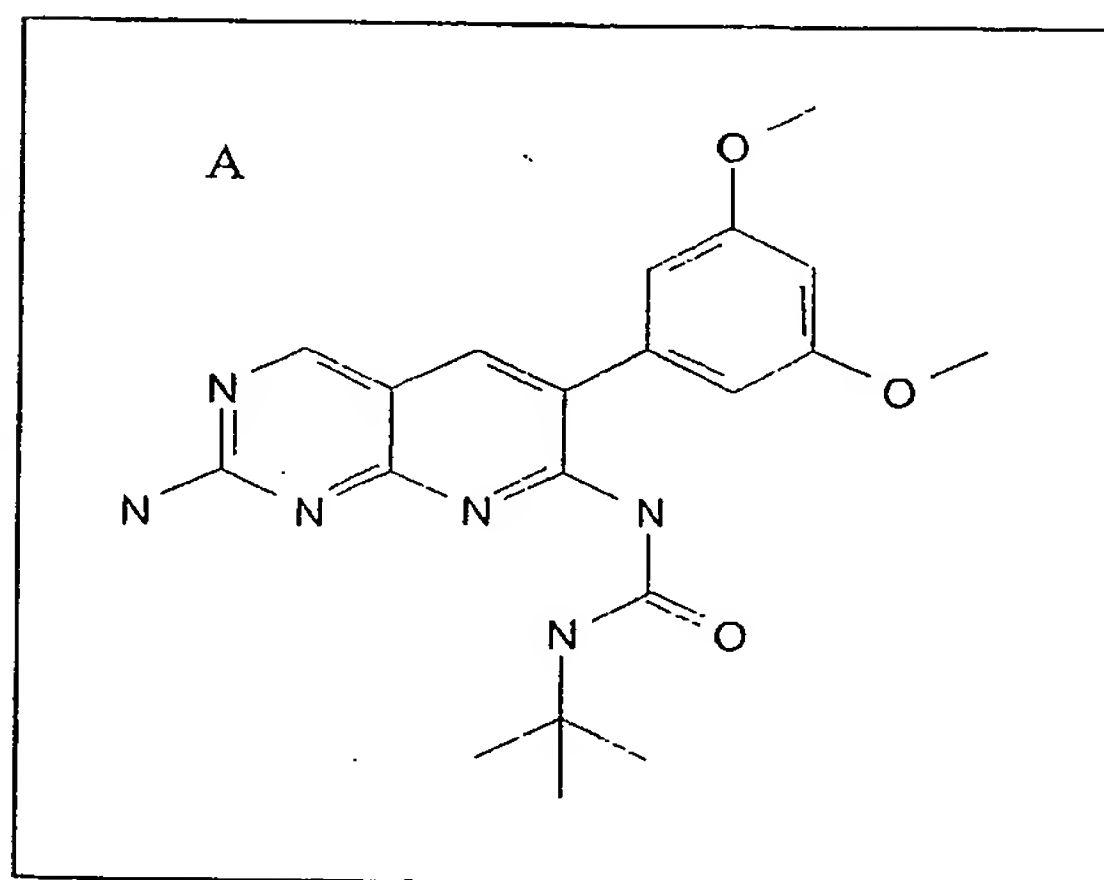
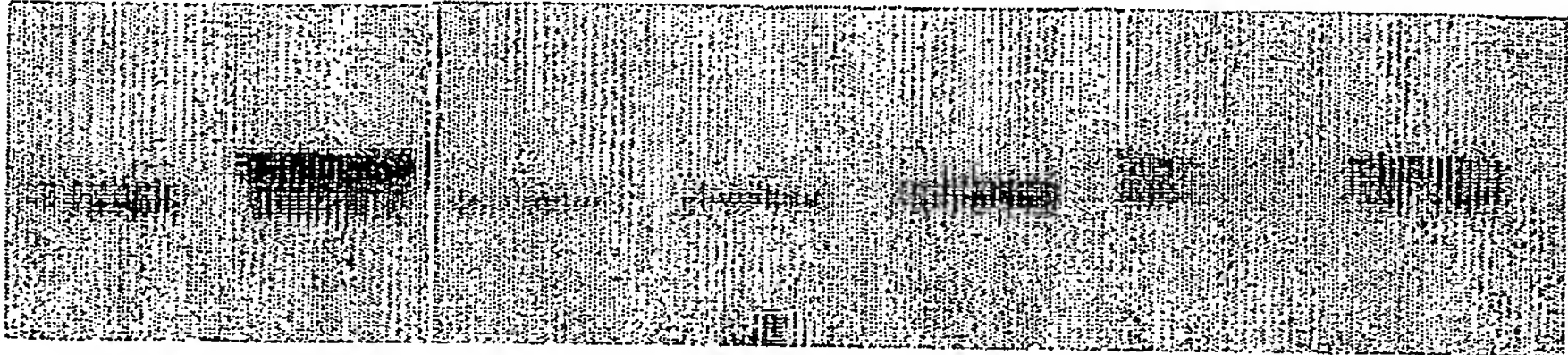
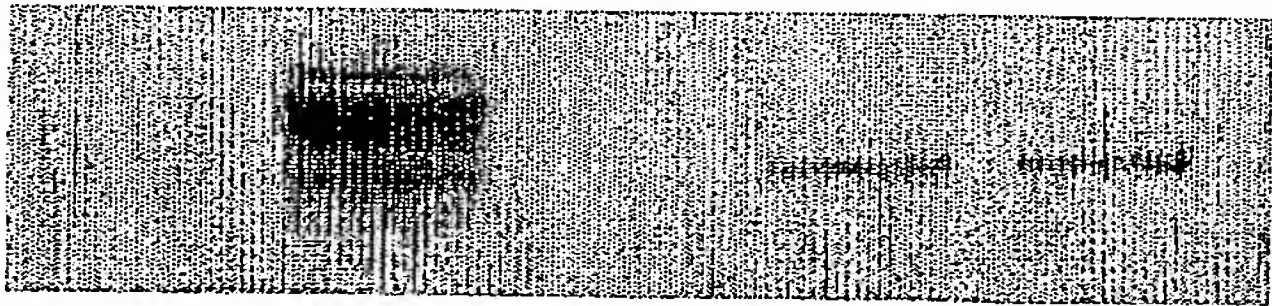


Fig. 31.

FGF	-	5 ng	5 ng	5 ng	5 ng	5 ng	5 ng
Pryimido-pyridines derivative A	-	-	0.5 μM	0.2 μM	0.1 μM	0.05 μM	0.02 μM



FGF	-	100 ng	100 ng	100 ng	100 ng
Pryimido-pyridines derivative B	-	-	0.1 μM	0.03 μM	0.01 μM



**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ **BLACK BORDERS**
- ☐ **IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- ☒ **FADED TEXT OR DRAWING**
- ☒ **BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- ☐ **SKEWED/SLANTED IMAGES**
- ☐ **COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- ☐ **GRAY SCALE DOCUMENTS**
- ☒ **LINES OR MARKS ON ORIGINAL DOCUMENT**
- ☒ **REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- ☐ **OTHER:** _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.